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CONVENTIONAL VERSUS NANOTECHNOLOGY FOR DRUG DELIVERY SYSTEM - A REVIEW

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ABSTRACT

Drug delivery systems (DDS) are a crucial area in pharmacology, ensuring proper delivery of therapeutic agents with enhanced efficacy and decreased side effects. Conventional drug delivery approach, which includes oral, parenteral, transdermal, and topical systems, has been widely employed but often suffers limitations such as poor bioavailability, non-specific targeting of drugs, and frequent dosing needs. The introduction of nanotechnology-based drug delivery systems (NDDS) has revolutionized the field, providing enhanced solubility, target specificity, controlled release, and decreased systemic toxicity. This review provides a comparative analysis of conventional and nanotechnology-based DDS, focusing on their mechanisms, advantages, limitations, and applications. Various nanocarriers like liposomes, dendrimers, polymeric nanoparticles, and metallic nanoparticles are being studied for the purpose of increasing drug solubility, bioavailability, and therapeutic activity. Moreover, the pharmacokinetic and pharmacodynamic properties of NDDS exhibit remarkable improvements in drug absorption, biodegradability, and elimination pathways. Although nanocarriers possess several advantages, they are confronted with challenges such as regulatory issues, toxicity concerns, scalability issues, and increased production costs. New Emerging trends in drug delivery, including AI-based nanocarrier design, personalized medicine, and smart drug delivery systems, have promising avenues to address these challenges. This review is based on the observations on the advancements in drug delivery technology, covering extensively their existing scenario, hurdles, and future scope in clinical practices.

INTRODUCTION

Overview of Drug delivery Systems (DDS)

Drug delivery systems (DDS) are a core technology in the field of pharmacology, aimed at facilitating improved distribution and action of drugs within the body. DDS involves the evaluation of pharmacokinetics and pharmacodynamics to comprehend how drugs are absorbed, distributed, metabolized, and excreted, as well as their impact on the body. DDS is significant in optimizing drug delivery by optimizing efficacy and minimizing side effects through targeted transport (Ezike et al., 2023).

Conventional Drug Delivery Systems

Conventional DDS have been crucial in improving therapeutic efficacy by managing the dose, time, and location of drug release. However, traditional systems lacked control over drug release, leading to inefficiency in drug absorption and distribution. To address such limitations, advancements such as coated technology and enteric coatings were established, improving drug stability and release patterns (Adepu & Ramakrishna, 2021a). Regardless of these advancements, conventional DDS still suffer from limitations such as poor bioavailability, non-specific targeting, and unwanted side effects.

Nanotechnology-Based Drug Delivery Systems

To address the drawbacks of conventional systems, nanotechnology-based DDS have emerged as a promising alternative. Nanotechnology is now being merged with Conventional DDS to enhance drug bioavailability, targeting, and controlled release. Various innovations, including RBC membrane-camouflaged nanoparticles, hyaluronic acid-based carriers, and polymer-lipid hybrid nanoparticles, have been engineered to maximize therapeutic efficacy, particularly in cancer therapy and other complex diseases (Parveen et al., 2023). These nanocarriers facilitate targeted drug delivery, reduce toxicity, and enhance treatment efficiency.

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Importance of effective drug delivery in healthcare

Effective drug delivery systems are vital in maximizing medical treatments and patient benefits. In the capacity to facilitate the drugs reaching the targeted site in the body, these systems significantly enhance therapeutic efficacy, resulting in improved treatment outcomes. Targeted drug delivery reduces exposure to off-target tissues, reducing toxicity and undesired side effects, which is an important aspect for potent medications (Ezike et al., 2023). Furthermore, drug delivery technologies that allow sustained-release formulations assist in increasing patient compliance by decreasing the dosing frequency, making regimens of treatment more convenient and simpler to adhere to.

Advanced drug delivery systems have also enabled emerging therapeutic strategies, such as the use of biologics and macromolecules that have specific delivery needs. Technologies like long-acting injectables have demonstrated immense potential in the cure of chronic conditions like HIV. Moreover, modern drug delivery approach focuses on overcoming complex physiological barriers, e.g., the blood-brain barrier or gastrointestinal tract, to enable the effective administration of a broader variety of therapeutic agents (Coelho et al., 2010). Personalized medicine is another emerging field benefiting from efficient drug delivery, as these technologies enable treatments tailored to individual patient needs, thereby enhancing efficacy while minimizing side effects.

The convergence of drug delivery with novel technologies such as machine learning and soft electronics will transform the field, becoming more precise and responsive to individual patient needs. More importantly, its global health relevance cannot be undervalued given that better formulations for drugs allow for therapies that are more within reach and are affordable, so health equity could be enhanced throughout the world (Vora et al., 2023). In summary, effective drug delivery systems optimize the therapeutic value of drugs, enhance patient compliance, facilitate novel therapies, and address the challenges posed by biological barriers, thus improving healthcare outcomes.

Evolution of drug delivery technology

The evolution of drug delivery technologies has progressed from conventional methods to advanced nanotechnology-based systems, which have significantly improved precision and efficiency in medical treatment. Traditionally, tablets, capsules, emulsions, suspensions were the first to pave the way for current advances. Nonetheless, these systems were plagued with problems like low solubility, poor bioavailability, and high drug aggregation, restraining their efficiency. The emergence of nanotechnology, initially envisioned by physicist Richard Feynman in 1959, revolutionized drug delivery with the capability to manipulate materials at the nanoscale (1-100 nm) (Y. Liu et al., 2024). This resulted in the creation of engineered nanoparticles, such as polymeric nanoparticles, liposomes, and carbon nanotubes, that enhance drug solubility, bioavailability, and targeted delivery. The shift from the micro to nano-scale drug delivery systems has also enabled the advent of controlled-release mechanisms, making use of erodible systems and hydrogels for extended therapeutic action. Moreover, recent innovations like microchips, microneedle-based transdermal systems, and ink-jet-printed microparticles are a drastic improvement over traditional methods, ensuring greater accuracy in drug delivery. The future of drug delivery is centered on scalable nano/micro manufacturing processes, aiming to further enhance targeted treatments and patient outcomes. This ongoing evolution highlights the significance of nanotechnology in determining the future of medicine, making treatments more effective and safer.

Objectives and Scope of the Review

This review will deliver a holistic view of the advancement of drug delivery technologies, more specifically, shifting from conventional systems to nanotechnology-based strategies. The main purpose is to compare traditional drug delivery methods—such as tablets, capsules, emulsions, and suspensions —with modern nanocarrier-based systems, highlighting their merits, demerits, along with their effects on therapeutic action (Fig. 1). In addition to this, the review also investigates the contribution of nanotechnology to overcome challenges associated with drug solubility, bioavailability, and targeted delivery. By examining key advancements in controlled-release mechanisms, microneedle-based transdermal delivery, and microchip-based drug delivery, this paper seeks to provide insights into existing innovations and their implications for a large-scale clinical use. The review encompasses future directions, with a focus on the advancements of scalable nano/micro manufacturing and its potential applications in precision medicine. Through such a review, the analysis will aim to enhance knowledge on how nanotechnology is transforming drug delivery, with the potential for better patient outcomes and future-proofing the field of pharmaceutical sciences.

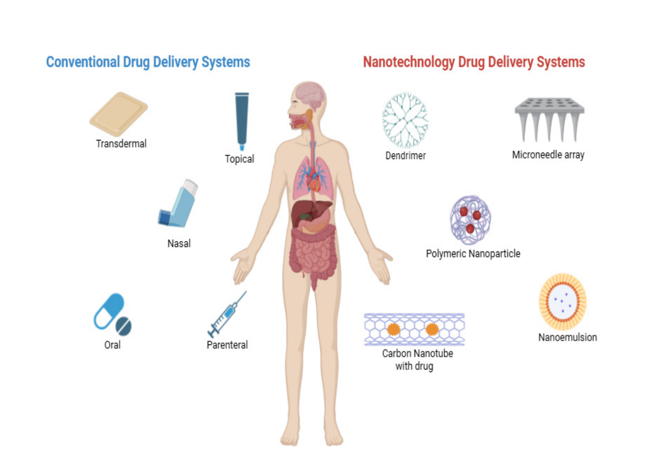

Figure 1. Conventional versus Nanotechnology Drug Delivery Systems

Conventional Drug Delivery Systems

Overview

Traditional drug delivery systems include traditional routes like oral (tablets, capsules, syrups), topical (ointments), and parenteral (intravenous, intramuscular) for delivery of active pharmaceutical ingredients (APIs). These systems are designed to provide therapeutic efficacy; however, they tend to suffer from drawbacks such as poor bioavailability, significant fluctuations in plasma drug levels, and the need for frequent dosing, which can result in suboptimal patient compliance (Adepu & Ramakrishna, 2021a). Traditionally, conventional DDS have been a cornerstone of pharmacotherapy, with early strategies being directed towards the mere administration of drugs without precise control over drug release. With time, pharmacokinetic advancements have resulted in the creation of controlled drug delivery systems to overcome the shortcomings of conventional methods. The mechanism of drug release in these systems includes absorption, distribution, metabolism, and elimination, all of which determine the therapeutic effect of the drug (Sultana et al., 2022). Rapid drug release in conventional DDS may lead to fluctuating drug concentrations, with the possibility of exceeding toxic levels or being below the minimum effective concentration, affecting treatment efficacy. Notwithstanding the limitations, conventional drug delivery is the foundation of contemporary medicine and the basis upon which advanced drug delivery technologies such as nanotechnology-based and controlled-release systems evolved, with a focus on maximizing efficacy, mitigating side effects, and enhancing patient compliance.

Types of Conventional Drug Delivery Systems

Conventional drug delivery systems are a heterogenous assortment of drug transport methods meant to deliver therapeutic drugs to their target sites within the body. These systems are differentiated by administration routes, each possessing particular advantages and constraints affecting drug performance, patient acceptability, and clinical effects (Tangboriboon, 2018). Major conventional drug delivery systems include oral, injectable, transdermal, pulmonary, rectal, and buccal/sublingual routes. The most common oral drug delivery is still in use because of the simplicity of administration, but it suffers from gastrointestinal degradation and unreliable bioavailability. Injectable delivery through subcutaneous, intramuscular, and intravenous methods circumvents the gastrointestinal tract, thus having higher bioavailability at the cost of administration by skilled personnel. Transdermal delivery offers a sustained release of drugs across the skin, escaping first-pass metabolism, but is restricted to molecules with suitable skin permeability. Pulmonary drug delivery, widely preferred in respiratory disorders, provides rapid absorption through the lungs but requires careful inhalation skills. Rectal administration is helpful for patients unable to take oral medications but is plagued by inconsistent absorption. Buccal and sublingual drug delivery allows speedy drug absorption via the oral mucosa while bypassing first-pass metabolism, but are limited to specific drugs and dosing (Hamzy et al., 2021). Understanding these conventional drug delivery systems is crucial for optimizing therapeutic strategies and creating novel formulations that improve drug action and patient compliance.

- **Oral Drug Delivery Systems-**

Oral drug delivery is the most commonly utilized method within conventional drug delivery systems due to its non-invasive nature, ease of administration, and high patient compliance. This method encompasses various formulations, including conventional tablets and capsules, liquid formulations, sustained-release systems, and emerging nanocarrier-based approaches. Conventional tablets and capsules remain the most widely used, offering ease of manufacturing and cost-effectiveness, though they often face bioavailability challenges due to solubility issues (Racaniello et al., 2024). Liquid formulations, such as solutions, suspensions, and emulsions, are preferred for patients with swallowing difficulties but may suffer from stability concerns. Sustained-release formulations enhance therapeutic efficacy by providing controlled drug release over an extended period, reducing dosing frequency and minimizing side effects (Adepu & Ramakrishna, 2021b). Additionally, advanced drug carriers, such as nanoparticles, micelles, and cyclodextrins, are being explored to improve drug solubility and stability in the gastrointestinal (GI) tract. Oral drug delivery systems play a vital role in the treatment of systemic and local gastrointestinal diseases. They are widely used for managing chronic conditions like diabetes and hypertension, as well as in pediatric formulations designed to enhance safety and efficacy. The advantages of oral drug delivery include its cost-effectiveness, non-invasiveness, and convenience, allowing patients to self-administer medications without healthcare assistance. However, several limitations impact its effectiveness. The primary challenge is low bioavailability, often due to poor solubility, GI permeability issues, and extensive first-pass metabolism, where drugs are metabolized in the liver before reaching systemic circulation. Additionally, physiological and biological barriers, such as enzymatic degradation, pH variations, and the presence of food, can significantly alter drug absorption (Stielow et al., 2023). Patient-related factors, including age, diet, and health status, further contribute to variability in drug response.

The mechanisms governing drug release in oral systems depend on physicochemical properties, GI permeability, and pharmacokinetics. Most conventional oral drugs rely on diffusion and erosion mechanisms for release, which influence their absorption and therapeutic effectiveness. Overcoming the challenges associated with oral drug delivery requires innovative formulation strategies. Advances in nanotechnology, bioavailability enhancers, and modified-release systems continue to improve drug stability, absorption, and therapeutic outcomes. While oral drug delivery remains a cornerstone of pharmacotherapy, ongoing research aims to refine its limitations and enhance its efficacy for a broader range of therapeutic applications (Y. Liu et al., 2024).

- **Parenteral Drug Delivery Systems**- Parenteral drug delivery systems play a crucial role in therapeutic interventions, particularly when oral administration is unsuitable due to factors like poor gastrointestinal absorption or the need for rapid drug action. These systems involve the direct administration of drugs into the body via various routes, including intravenous (IV), intramuscular (IM), and subcutaneous (SC) injections (Taneja et al., 2018). The IV route delivers drugs directly into the bloodstream, ensuring 100% bioavailability and immediate therapeutic effects, making it ideal for emergency situations. The IM route deposits drugs into muscle tissue, allowing for a slower but sustained release, commonly used for vaccines and long-acting medications. The SC route, which involves injecting drugs into the fatty tissue beneath the skin, provides an even slower absorption rate and is frequently used for insulin and biologic therapies (Kim & Jesus, 2023). Despite their effectiveness, conventional parenteral drug delivery systems face several challenges. Maintaining therapeutic drug levels can be difficult due to rapid absorption and elimination, leading to fluctuations in plasma concentration that may result in sub-therapeutic or toxic effects. Additionally, frequent injections can reduce patient compliance, and the inability of conventional parenteral systems to provide sustained drug release further complicates long-term treatment. The pharmacokinetics of parenteral administration often exhibit an initial surge in plasma drug concentration followed by a rapid decline, necessitating multiple doses to maintain therapeutic efficacy. Moreover, systemic exposure to high drug concentrations increases the risk of adverse effects (Fernandez et al., 2011). Parenteral drug delivery is widely applied in acute and chronic disease management, including emergency medicine, pain management, oncology, diabetes, and vaccination. While IV infusions and injections remain the most commonly used methods, advancements in controlled drug delivery systems, such as implantable devices and infusion pumps, are being explored to overcome the limitations of conventional approaches. These advanced systems aim to improve therapeutic efficacy by maintaining consistent drug levels, reducing dosing frequency, and enhancing patient adherence. The continuous evolution of parenteral drug delivery strategies is crucial for optimizing treatment outcomes and minimizing the drawbacks associated with traditional methods (Y. Liu et al., 2024).

- **Transdermal Drug Delivery Systems**– Transdermal drug delivery systems (TDDS) provide an innovative and non-invasive approach to drug administration by enabling the controlled release of medications through the skin into the bloodstream. These systems offer several advantages over traditional oral and parenteral routes, including improved patient compliance, steady plasma drug levels, and reduced gastrointestinal side effects (Alkilani et al., 2015). TDDS primarily include transdermal patches, which are composed of multiple layers: a protective backing film, a drug-containing layer, a diffusion-controlling membrane, and an adhesive layer ensuring proper skin adherence. The drug release mechanism relies on passive diffusion or active enhancement techniques, such as chemical permeation enhancers, microneedles, and iontophoresis, to improve skin permeability and facilitate drug absorption (W. Y. Jeong et al., 2021). TDDS find extensive applications in chronic pain management, hormonal therapies, nicotine replacement, and non-invasive vaccine administration. These systems ensure prolonged therapeutic effects by maintaining consistent drug concentrations in the bloodstream, thereby reducing fluctuations seen in oral drug delivery. However, despite their advantages, TDDS face limitations such as restricted applicability to drugs with suitable molecular weight and lipophilicity, potential skin irritation, and variability in drug absorption due to individual differences in skin condition, age, and hydration (Alkilani et al., 2015). Additionally, TDDS are not ideal for acute pain management due to their slow drug absorption and delayed onset of action. From a pharmacokinetic and pharmacodynamic perspective, TDDS aim to optimize drug bioavailability while maintaining a steady therapeutic effect, minimizing peak-and-trough fluctuations often observed with oral administration. Ongoing research focuses on enhancing the efficiency of TDDS by developing advanced formulations, hybrid systems, and novel enhancement techniques to broaden the range of drugs suitable for transdermal administration (W. Y. Jeong et al., 2021). While TDDS represent a significant advancement in drug delivery, overcoming their current limitations remains crucial for expanding their clinical applications and improving patient outcomes.
- **Topical Drug Delivery System-** Topical drug delivery systems have emerged as an effective method for localized treatment, offering advantages such as ease of administration, targeted action, and improved patient compliance. These systems are designed to deliver therapeutic agents directly to the skin or mucous membranes, making them particularly useful for dermatological, analgesic, and hormonal therapies (Zhao et al., 2024). This review discusses the various types, methods of administration, applications, and challenges associated with topical drug delivery system. Furthermore, it highlights the potential of in situ gelling formulations as an innovative approach to enhance drug retention and efficacy in topical treatments. Topical drug delivery systems play a crucial role in modern pharmacology, providing an alternative to oral and systemic drug delivery. By directly applying medications to the site of action, these systems minimize systemic side effects and maximize local therapeutic effects (Zhao et al., 2024). However, several challenges, including skin penetration barriers and formulation limitations, must be addressed to optimize their effectiveness. This review provides an overview of topical drug delivery systems, their mechanisms, and advancements in in situ gelling drug delivery systems. Conventional topical drug delivery systems include creams, gels, ointments, and transdermal patches, each offering distinct advantages based on their composition and application. Creams are emulsions that can be either oil-in-water or water-in-oil, commonly used for moisturizing, wound healing, and delivering active pharmaceutical ingredients (Hamzy et al., 2021). Gels are semi-solid formulations with a cooling effect and quick absorption, making them ideal for dermatological conditions and localized pain relief. Ointments, being greasy preparations, provide an occlusive barrier that prevents moisture loss and ensures prolonged drug contact, making them effective for dry skin conditions and wound healing. Transdermal patches, on the other hand, enable controlled drug release over an extended period, allowing steady absorption through the skin into systemic circulation, which is beneficial for chronic treatments such as hormone replacement therapy(Alkilani et al., 2015). Despite their widespread use, these conventional systems face challenges such

as limited drug penetration through the stratum corneum and variability in skin conditions, which can impact their efficacy. Overcoming these barriers requires formulation optimization and novel delivery approaches to enhance drug bioavailability and therapeutic outcomes. The administration of topical drug delivery systems can be categorized into two main approaches: Drugs are applied directly to the affected area, ensuring localized action. This method is commonly used for treating skin disorders, wounds, and infections. Involves the penetration of drugs through the skin into systemic circulation (Zhao et al., 2024). This method is employed for sustained drug release and is commonly used in patches and advanced gel formulations. Topical drug delivery is advantageous for various therapeutic areas, including: Topical formulations are widely used for treating conditions such as eczema, psoriasis, acne, and fungal infections Topical analgesics, including gels and patches, are effective for localized pain relief in conditions such as arthritis, muscle strains, and neuropathic pain. Transdermal patches are used for hormone replacement therapy (HRT), ensuring a controlled and steady release of hormones into the bloodstream. In situ gelling systems have garnered attention in topical drug delivery due to their ability to transition from a liquid to a gel state upon application (Derry et al., 2017). Key advantages of these systems include: Mucoadhesive polymers prolong drug contact at the target site, improving therapeutic outcomes. These systems enable sustained drug release, minimizing dosing frequency and enhancing patient compliance. The liquid state at ambient conditions facilitates easy administration, including as sprays or drops. Despite their benefits, topical drug delivery systems face several challenges: The stratum corneum serves as a major barrier to drug absorption, limiting the effectiveness of certain formulations. Factors such as skin hydration, temperature, and integrity influence drug absorption and bioavailability. Developing formulations with optimal rheological properties and stability remains a significant hurdle in translating research into clinical applications (Yu et al., 2021). Topical drug delivery systems offer an effective means of delivering medications directly to the site of action, minimizing systemic side effects and improving patient adherence. Innovations such as in situ gelling drug delivery systems present promising advancements in enhancing drug retention and controlled release. However, challenges related to formulation stability, skin penetration, and bioavailability must be addressed to fully realize the potential of these systems in clinical applications. Future research should focus on optimizing formulations and developing novel approaches to overcome these limitations.

- **Ocular Drug Delivery Systems-** Conventional ocular drug delivery systems, including eye drops, ointments, gels, and ocular inserts, are widely used for treating various eye diseases such as conjunctivitis, glaucoma, cataracts, diabetic retinopathy, and age-related macular degeneration. Among these, eye drops dominate the market, accounting for over 70% of prescription medications due to their ease of application and noninvasive nature (Gabai et al., 2023). Despite their widespread use, conventional ocular drug delivery systems face significant challenges, primarily due to poor bioavailability. Only about 5% of the drug from eye drops reaches ocular tissues due to rapid tear drainage, blinking, and the presence of physiological barriers such as the cornea, conjunctiva, and blood-retinal barrier, which hinder effective drug penetration (Gabai et al., 2023). Additionally, frequent administration is required to maintain therapeutic drug levels, leading to poor patient compliance. Alternative methods, such as intraocular and periocular injections, improve drug delivery to the posterior segment but are invasive and associated with potential complications. Sustained-release systems, such as in situ gels and ocular implants, have been explored to enhance drug retention and bioavailability (Patel et al., 2013). However, challenges such as patient discomfort, blurred vision, and the need for surgical implantation remain. Despite their limitations, conventional ocular drug delivery systems continue to be the primary choice for localized eye treatments, minimizing systemic side effects. To overcome their drawbacks, innovative drug delivery approaches are needed to enhance drug residence time, permeability, and therapeutic efficacy, ultimately improving patient outcomes in ocular therapeutics.
- **Nasal Drug Delivery Systems**- Nasal drug delivery is emerging as a promising alternative to conventional drug administration, particularly for targeting the brain and achieving rapid systemic effects. This route utilizes the unique anatomical and physiological characteristics of the nasal cavity to facilitate drug absorption while bypassing first-pass metabolism and the blood-brain barrier (S. H. Jeong et al., 2022). Drugs administered nasally can reach the brain through direct pathways, such as the olfactory nerve, or indirectly via systemic circulation. The method is widely used for treating allergies, migraines, neurological disorders like Alzheimer’s and epilepsy, and even for systemic conditions such as diabetes, where nasal insulin delivery provides a non-invasive alternative to injections (S. H. Jeong et al., 2022). Additionally, nasal vaccines like FluMist® highlight its potential in immunization. Key advantages of nasal drug delivery include its non-invasive nature, rapid onset of action due to the rich vascularization of the nasal mucosa, and the ability to provide localized treatment for neurological disorders with reduced systemic side effects. However, this approach faces limitations such as low drug permeability, rapid mucociliary clearance, and formulation stability challenges, which can affect drug absorption and therapeutic efficacy. Some formulations may also cause nasal irritation, impacting patient compliance. To address these challenges, ongoing research is focused on innovative solutions, including the use of nanocarriers, mucoadhesive agents, and hyper gravity techniques to enhance drug permeability and retention time (Huang et al., 2024). Additionally, high-concentration injectables are being developed to improve drug efficacy. Overall, while nasal drug delivery presents significant advantages over conventional methods, continued advancements in for-

mulation strategies and drug delivery technologies are essential to optimize its therapeutic potential and expand its clinical applications.

- **Rectal and Vaginal Drug Delivery Systems**- Rectal and vaginal drug delivery systems play a crucial role in conventional drug delivery, offering unique advantages for local and systemic treatments while addressing challenges related to patient compliance and drug absorption. Rectal administration involves suppositories, enemas, and gels, making it a viable alternative for patients who cannot take oral medications due to nausea, vomiting, or unconsciousness (Osmałek et al., 2021). This route is effective for treating conditions like hemorrhoids, constipation, and systemic diseases requiring rapid drug absorption. Vaginal drug delivery, on the other hand, utilizes tablets, creams, gels, and rings for localized treatments, such as infections, hormonal therapies, and contraception. Both methods benefit from bypassing first-pass metabolism, leading to improved bioavailability of certain drugs (Osmałek et al., 2021). However, limitations include variability in drug absorption due to factors like rectal fluid content, fecal matter, menstrual cycle influences, and vaginal flora changes. Patient discomfort and formulation leakage further impact compliance. To overcome these challenges, innovative strategies such as mucoadhesive gels, nanoparticles, and controlled-release formulations are being developed to enhance drug retention and absorption (Coelho et al., 2010). Additionally, patient education plays a key role in improving adherence to these delivery systems. Despite their challenges, rectal and vaginal drug delivery systems provide essential therapeutic benefits, particularly for individuals who require alternative routes of administration, and ongoing research aims to optimize their effectiveness in clinical practice.

1.1. Pharmacokinetics and Pharmacodynamics of Conventional Drug delivery Systems:

Pharmacokinetics and pharmacodynamics are central to comprehending the therapeutic effectiveness of conventional drug delivery systems (CDDS). **Pharmacokinetics** is a term used to describe the course of a drug in the body, involving four major processes: **absorption**, **distribution**, **metabolism**, and **excretion** (Glassman & Muzykantov, 2019). Absorption will dictate how the drug is released into the bloodstream from the point of administration, while distribution encompasses the spreading of the drug in tissues and body fluids. Metabolism, which takes place mainly in the liver, biochemically converts the drug into active or inactive metabolites, and excretion removes the drug via urine, feces, or other pathways. The pharmacokinetic pattern of CDDS is usually characterized by **bolus pharmacokinetics**, where rapid drug absorption results in fluctuating plasma drug concentrations, often less than minimum effective concentration (MEC) or exceeding toxic thresholds (Fernandez et al., 2011). These variations require more **frequent dosing**, which is a challenge to patient compliance and increases the risk of side effects. Factors such as the **route of administration**, **physicochemical properties of the drug**, and **drug formulation** have a significant impact on the pharmacokinetics of CDDS. **Pharmacodynamics, however,** investigates the biological effects of the drug and mechanisms of action, defining the correlation between drug concentration and therapeutic response (Glassman & Muzykantov, 2019). Traditional drug delivery systems do not usually have **controlled release mechanisms**, which may result in unreliable drug effects and potential side effects. These drawbacks make it necessary for **advanced drug delivery systems** that will deliver drugs sustainably, with targeting, in a more predictable manner. Research on controlled drug delivery technology continues to address pharmacokinetic and pharmacodynamic profiles, maximizing therapeutic response while mitigating side effects.

1.2. Applications of Conventional Drug Delivery Systems:

Conventional drug delivery systems (CDDS) are very essential in the delivery of drugs in different fields of medicine. The systems are very common because of their proven efficacy, simplicity of use, and affordability (Hamzy et al., 2021). **Oral drug delivery**, the most prevalent one, comprises tablets, capsules, and syrups, and hence is applicable for a wide variety of diseases, ranging from chronic conditions such as hypertension and diabetes (Kim & Jesus, 2023; Stielow et al., 2023). **Injectable drug delivery** routes, such as intravenous (IV), intramuscular, and subcutaneous injections, are critical for instantaneous drug action, particularly in emergencies, chemotherapy, and vaccine delivery (Kim & Jesus, 2023). **Topical drug delivery**, including creams, ointments, and transdermal patches, ensures localized treatment for skin ailments and controlled release of drugs from the systemic circulation for pain management and hormone replacement(Zhao et al., 2024). **Pulmonary drug delivery**, via inhalers and nebulizers, is essential for the treatment of respiratory disorders such as asthma and chronic obstructive pulmonary disease (COPD), providing direct action of the drug in the lungs with minimal side effects on the system (S. H. Jeong et al., 2022). **Rectal and vaginal drug delivery** systems, including suppositories and inserts, are useful for patients who are unable to take oral medications, providing effective therapy for local conditions and systemic absorption in pain relief.

In **chronic disease management**, CDDS plays a critical role in long-term treatment regimens, especially for conditions such as cardiovascular diseases, diabetes, and psychiatric disorders, where patient compliance and sustained drug levels are essential. **Pain management** is dependent on several CDDS, such as oral analgesics, transdermal patches for extended relief, and injections for instant pain relief. **Cancer treatment** employs IV injections for chemotherapy, to deliver anticancer drugs with accurate dosing and systemic distribution, while controlled-release formulations reduce side effects and enhance patient comfort (Adepu & Ramakrishna, 2021b). Although widely used, CDDS are hampered by erratic drug absorption, the need for frequent dosing, and the risk of side effects, calling for the need of advanced drug delivery systems to optimize treatment effectiveness and patient response.

1.3. Advantages of Conventional Drug delivery systems:

Conventional drug delivery systems (CDDS) possess several benefits that have established them as the backbone of pharmacotherapy for decades. Their **cost-effectiveness** is one of the main advantages, as traditional formulations such as tablets, capsules, and injections are relatively inexpensive to produce compared to advanced drug delivery systems (Sultana et al., 2022). This makes them widely accessible, especially in low-resource environments, to cover a wider population of patients. Also, CDDS are facilitated by **easy formulation and manufacturing**, as their established production methods involve little specialized technology, which enables mass production and uniform quality control. Another significant advantage is their **well-established clinical use**, with extensive research, regulatory approvals, and decades of real-world application providing a strong foundation for their safety and efficacy. Healthcare providers and patients are well aware of traditional dosage forms, and this makes prescribing and administration easy, resulting in **excellent patient compliance**. Additionally, CDDS have a variety of **administration routes**, including oral, injectable, topical, and transdermal, permitting flexibility in treatment regimens for various diseases and patient requirements (Kim & Jesus, 2023). The fact that standardized dosing regimens and well-characterized pharmacokinetics are available makes them reliable in clinical use. Despite certain limitations, conventional drug delivery systems continue to be a part of contemporary medicine, yielding effective, affordable, and well-documented treatments for several acute and chronic ailments.

1.4. Limitations of Conventional Drug Delivery Systems:

Although they have been extensively applied, conventional drug delivery systems (CDDS) face several limitations impacting their therapeutic efficacy and patient compliance (Hamzy et al., 2021). One key disadvantage is **reduced bioavailability**, especially for orally administered drugs, where first-pass metabolism and the rate of drug elimination can reduce the drug delivery to systemic circulation considerably (Table 1). This often results in suboptimal therapeutic effects, necessitating higher doses to establish the desired response. Another major issue is **non-specific targeting**, wherein drugs spread across the body instead of being active only at the desired location. This indiscriminate distribution can result in **undesirable side effects** and potential toxicity in off-target tissues, restricting the safety and accuracy of treatment (Sultana et al., 2022). Moreover, many traditional drugs have a **short plasma half-life**, demanding frequent administration to maintain therapeutic levels. Such repeated dosing regimens not only tax patients but also pose a risk of omitted doses, causing irregular drug levels and decreased effectiveness. In addition, **drug degradation in biological fluids** is a concern, as certain medications are unstable in the physiological environment because of enzymatic degradation or pH-dependent degradation (Stielow et al., 2023). This instability can cause diminished drug potency even before it reaches the target site. These issues point to the necessity of sophisticated drug delivery systems that maximize bioavailability, provide targeted delivery, extend drug circulation time, and optimize overall treatment outcomes.

Table 1. Comparative Bioavailability Values (%) of Drug Delivery Systems

Drug Delivery System	Bioavailabil
Intravenous injection	100%
Nanocarrier-based Drug Delivery System	80-90%
Oral Drug Delivery System	20-40%
Transdermal Drug Delivery System	50-70%
Nasal Drug Delivery System	50-60%
Rectal/Vaginal Drug Delivery System	30-50%

3. Nanotechnology-Based Drug Delivery Systems

3.1. Overview:

Nanotechnology has transformed drug delivery by transcending the shortcomings of traditional approaches, providing targeted therapy, improved bioavailability, and controlled release. **Nanotechnology-driven drug delivery systems** employ nanomaterials at the nanoscale to enhance therapeutic effects through effective drug delivery, minimizing toxicity, and drug stabilization (Y. Liu et al., 2024). **Nanoparticles (NPs)** are central to these new delivery systems, as they can be designed to alter size, surface characteristics, and composition to confer targeted and sustained drug release. Through encapsulation of therapeutic agents, NPs increase drug solubility, extend circulation time, and shield drugs from enzymatic degradation. This is particularly beneficial for hydrophobic drugs, which have difficulty with low bioavailability in conventional formulations (Egwu et al., 2024). Furthermore, NPs facilitate **targeted drug delivery**, which takes therapeutic agents to diseased tissues and minimizes systemic side effects—a significant step for the treatment of diseases such as cancer and resistant infections. **Liposomes, micelles, dendrimers, quantum dots, carbon nanotubes, and metal-based nanoparticles** are some of the nano-carriers that have been extensively studied in drug delivery systems. **Controlled release mechanisms** are also provided by these systems, which prolongs the therapeutic effects while decreasing the frequency of dosing and enhancing patient compliance(Adepu & Ramakrishna, 2021b). Despite such merits, obstacles in terms of **regulatory hurdles, scalability, cost, and possible toxicity** should be overcome in their universal application at the clinic level. Nanotechnology-based drug delivery, while improving constantly as technology evolves, carries gigantic promises of revolutionizing today's medicine in its improved drug efficacy and its patients' outcome in alleviating conditions chronic and disease-tous in nature.

3.2. Types of Nanotechnology Based Drug Delivery Systems:

- **Liposomes**- Liposomes have become a very effective and versatile nanotechnology-based delivery system, with many benefits in enhancing drug efficacy and safety. These **self-assembled, phospholipid-based vesicles** are made up of one or more lipid bilayers encapsulating an aqueous core and can surround both **hydrophilic and hydrophobic drugs** (P. Liu et al., 2022). Their capacity to shield drugs from enzymatic degradation increases drug stability and **bioavailability** and makes them especially useful for the delivery of sensitive therapeutic agents. Liposomes enhance **solubilization** of poor water-soluble drugs and facilitate **controlled drug release**, so that sustained action is maintained along with reduced variation in drug levels (Nsairat et al., 2022). **Targeting ability** also advances therapeutic specificity—passive targeting takes advantage of the **increased permeability and retention (EPR) effect** for liposomes to be localized at tumor sites, whereas **active targeting** entails surface customization with ligands or antibodies so that site-specific delivery of drug is ensured (Patra et al., 2018). Liposomes have been used extensively in **cancer treatment, vaccine, and antimicrobial therapy**, with FDA-approved drugs showcasing their therapeutic potential. Nevertheless, drawbacks including **stability issues, potential drug leakage, and high production costs** remain barriers to extensive usage. Yet with ongoing research continuing to fine-tune liposomal formulations, there is further strength in their positioning as a leading vehicle in **contemporary drug delivery strategies**.

- **Polymeric Nanoparticles-** Polymeric nanoparticles are a highly versatile and effective **nanotechnology-based drug delivery system**, offering **controlled drug release, enhanced bioavailability, and targeted delivery** (Begines et al., 2020**).** Polymeric nanoparticles are generally made of **biodegradable and biocompatible polymers** to provide safe and effective drug encapsulation. Based on their structural features, polymeric nanoparticles are categorized into **solid polymeric nanoparticles, polymeric micelles, polymer-drug conjugates, dendrimers, polymersomes, polyplexes, nanoliposomes, and nanoniosomes** (Patra et al., 2018). Each of these categories plays a special role in drug solubility, stability, and controlled release improvement. Various **fabrication techniques** such as **solvent evaporation, emulsion polymerization, nanoprecipitation, and electrospinning** are employed to prepare these nanoparticles, ensuring uniform size and efficient drug loading. The drug delivery mechanism using polymeric nanoparticles includes **drug encapsulation to prevent degradation, controlled release to maintain therapeutic concentrations, surface modifications for active targeting, and improved solubility for enhanced bioavailability** (Patra et al., 2018). These nanoparticles are also designed to deliver drugs through **diffusion, swelling, or polymer erosion** to achieve sustained drug activity. Their application spans across **cancer therapy, gene delivery, vaccine development, and the delivery of poorly soluble drugs**, making them a crucial innovation in modern pharmaceuticals (Begines et al., 2020). However, challenges such as **polymer toxicity, large-scale production limitations, and regulatory hurdles** need to be addressed for broader clinical translation. Despite all these challenges, ongoing research and developments in the fields of polymer chemistry and nanotechnology are promising polymeric nanoparticles to transform **personalized medicine and targeted therapies**, offering **safer, more efficient, and patient-friendly drug delivery solutions** (Adepu & Ramakrishna, 2021b).

- **Solid-Lipid Nanoparticles-** Solid lipid nanoparticles (SLNs) have emerged as a promising drug delivery system due to their unique physicochemical properties, biocompatibility, and ability to enhance the therapeutic efficacy of encapsulated drugs. These nanoparticles, composed of solid lipids that remain stable at room and body temperatures, provide controlled and sustained drug release while improving drug solubility and bioavailability (Arabestani et al., 2024). SLNs can be classified into different models based on their structural organization, including the drug-enriched shell model, the homogeneous matrix model, and the drug-enriched core model, each influencing drug release kinetics. Additionally, nanostructured lipid carriers (NLCs), an advanced version of SLNs, incorporate liquid lipids into the solid lipid matrix, enhancing encapsulation efficiency and preventing drug expulsion during storage . Various preparation methods, such as high-pressure homogenization, ultrasonication, solvent evaporation, and microemulsion techniques, enable precise control over particle size, drug loading, and stability (Arabestani et al., 2024). The release of drugs from SLNs occurs through diffusion, dissolution, and erosion of the lipid matrix, allowing for tailored therapeutic effects. One of the most significant advantages of SLNs is their ability to cross biological barriers, particularly the blood-brain barrier (BBB), making them highly suitable for central nervous system (CNS) drug delivery (Satapathy et al., 2021). This property has positioned SLNs as a potential tool for treating neurodegenerative disorders, brain tumors, and other CNS-related conditions. Furthermore, their biocompatibility and reduced toxicity make them an attractive alternative to polymeric nanoparticles for various biomedical applications, including cancer therapy, gene delivery, and antiviral treatments. Despite their numerous advantages, challenges such as long-term stability, large-scale production, and potential cytotoxicity of certain lipid formulations must be addressed for successful clinical translation (Arabestani et al., 2024). Ongoing research efforts focus on optimizing lipid compositions, surface modifications, and targeting strategies to improve SLN-based drug delivery systems. The integration of SLNs with advanced technologies, such as ligand-based targeting, stimuli-responsive drug release, and combination therapy approaches, holds immense potential for revolutionizing precision medicine and enhancing therapeutic outcomes in various diseases (M et al., 2024).

- **Dendrimers-** Dendrimers are highly branched, nanoscale macromolecules with a well-defined structure comprising a central core, repeating branching units, and terminal functional groups. This unique architecture provides them with exceptional advantages in drug delivery, including precise size control, multivalency, and high drug-loading capacity (Chabre & Roy, 2010). Their internal cavities allow for the encapsulation of hydrophobic drugs, while the surface functional groups enable the conjugation of hydrophilic drugs, targeting ligands, and imaging agents, enhancing solubility and bioavailability. Dendrimers employ multiple drug delivery mechanisms, including passive diffusion, receptor-mediated endocytosis, and stimuli-responsive drug release, making them highly adaptable for controlled and targeted therapies. Advances in dendrimer-based formulations have led to the development of responsive delivery systems that release drugs in response to pH, temperature, or enzyme activity, optimizing therapeutic efficacy (Abbasi et al., 2014). Furthermore, dendrimer hydrogels have emerged as an innovative approach for sustained drug release in localized treatments. Despite their significant potential, challenges such as cytotoxicity, complex synthesis, and regulatory barriers must be addressed for successful clinical translation. Recent studies have focused on modifying dendrimer surfaces with polyethylene glycol (PEG) and other biocompatible polymers to reduce toxicity and improve circulation time. The integration of dendrimers with combination therapies, gene delivery, and diagnostic applications positions them as a transformative platform in precision medicine (Abbasi et al., 2014). With ongoing research aimed at overcoming current limitations, dendrimers hold immense promise in revolutionizing nanomedicine and improving therapeutic outcomes across a wide range of diseases.

- **Nano-emulsions-** Nano-emulsions, a class of nanotechnology-based drug delivery systems, are thermodynamically stable, heterogeneous mixtures of oil and water stabilized by surfactants, with droplet sizes typically ranging from 20 to 200 nm. These nanosized emulsions offer significant advantages in drug delivery, particularly for hydrophobic drugs, by enhancing solubility, bioavailability, and targeted distribution (McClements, 2021). The small droplet size increases surface area, facilitating efficient absorption and penetration through biological membranes, thereby improving therapeutic efficacy compared to conventional emulsions. Nano-emulsions have been explored for multiple routes of administration, including oral, intravenous, and topical applications, allowing for versatile pharmaceutical use (Preeti et al., 2023). Recent advancements have demonstrated their potential in encapsulating a wide range of therapeutic agents, including small molecules, peptides, and nucleic acids, broadening their applicability in modern medicine. Stability remains a critical challenge in nano-emulsion formulation, as factors such as oil-to-water ratio, surfactant concentration, and gelling agents influence their physicochemical properties, including particle size, polydispersity index (PdI), and zeta potential (Preeti et al., 2023). Innovative formulation strategies, such as organogels and advanced surfactant systems, have been developed to enhance nano-emulsion stability and ensure controlled drug release. In vitro and in vivo studies further validate the biocompatibility and therapeutic potential of nano-emulsions, with research showing their ability to reduce tumor volume in cancer models and maintain cell viability in hepatocyte studies (Preeti et al., 2023). Despite these advantages, challenges such as potential surfactant toxicity, regulatory complexities, and large-scale production limitations must be addressed to facilitate clinical translation. With ongoing research and technological advancements, nano-emulsions are poised to revolutionize drug delivery, offering a promising platform for improving the efficacy, safety, and precision of therapeutic interventions across various medical fields (McClements, 2021).

- **Carbon-Based Nanoparticles-** Carbon-based nanoparticles (CBNs), including carbon nanotubes (CNTs), graphene, nanodiamonds, fullerenes, porous carbon, and carbon dots, have emerged as promising nanomaterials in drug delivery and biomedical applications. These nanoparticles possess unique physicochemical properties such as high surface area, excellent drug-loading capacity, and the ability to penetrate biological membranes, making them efficient carriers for therapeutic agents (Jayaprakash et al., 2024). Based on their structural composition, CBNs are categorized into different types, with CNTs, graphene, and fullerenes being widely utilized in biomedical research. Among them, carbon nanotubes play a significant role in drug delivery and cancer therapy (Debnath & Srivastava, 2021). They can be classified into single-walled carbon nanotubes (SWCNTs), which have a diameter of 5–15 nm and are used for gene delivery, imaging, and targeted therapy, and multi-walled carbon nanotubes (MWCNTs), composed of multiple graphene layers, which enhance drug delivery efficiency. Functionalized CNTs have been used to transport anticancer drugs such as paclitaxel and methotrexate, often conjugated with targeting ligands like folic acid to improve specificity. Additionally, CNTs exhibit strong near-infrared (NIR) light absorption properties, making them effective in photothermal therapy for drug-resistant cancer cells (Debnath & Srivastava, 2021). Beyond oncology, mesoporous carbon nanoparticles have been employed to improve the oral bioavailability of poorly soluble drugs by enhancing their dissolution rates in gastric fluids. Moreover, CBNs demonstrate significant potential in neurological applications due to their ability to cross the blood-brain barrier (BBB). Functionalized CNTs loaded with levodopa have been developed for targeted drug transport to the nervous system, offering potential therapeutic strategies for neurodegenerative diseases such as Parkinson's (Jayaprakash et al., 2024). Furthermore, biomedical imaging has benefited from the use of CNTs, improving diagnostic accuracy in diseases like breast cancer. Despite their numerous advantages, CBNs face challenges, including potential toxicity, complex synthesis, and regulatory hurdles. Studies indicate that MWCNTs may induce cell death in certain biological systems, while functionalization techniques, such as surface modifications and biopolymer coatings, can enhance biocompatibility and reduce toxicity. Temperature-responsive biomolecule release systems, such as chitosan-functionalized CNTs, have demonstrated controlled drug release mechanisms, further advancing their application in medicine (Egwu et al., 2024). However, concerns regarding inflammation, pulmonary fibrosis, and DNA damage remain, necessitating further research to optimize safety profiles. The future of CBNs in drug delivery and nanomedicine depends on advancements in functionalization techniques, toxicity assessments, and large-scale synthesis methods. Their potential to enhance targeted therapy, improve drug bioavailability, and enable personalized medicine highlights their significance in modern healthcare. With continued research, CBNs could revolutionize drug delivery systems, paving the way for innovative therapeutic strategies in cancer treatment, neurodegenerative disorders, and beyond (Egwu et al., 2024).

- **Metallic Nanoparticles**- Metallic nanoparticles (MNPs) have emerged as promising tools in drug delivery and nanomedicine due to their unique physicochemical properties, which enhance drug solubility, bioavailability, and targeted therapy. Various types of metallic and metal oxide nanoparticles are employed for biomedical applications (Chandrakala et al., 2022). **Silver (Ag) nanoparticles** are widely recognized for their antimicrobial properties and are used in wound healing, cancer therapy, and antimicrobial coatings. **Gold (Au) nanoparticles** are highly biocompatible with tunable optical properties, making them ideal for targeted drug delivery, photothermal therapy, and biomedical imaging. **Iron oxide (Fe□O□) nanoparticles** exhibit magnetic properties that enable controlled drug release via external magnetic fields and are commonly used in cancer therapy, MRI contrast imaging, and hyperthermia treatments. Similarly, **zinc oxide (ZnO) nanoparticles** possess antibacterial, anticancer, and antioxidant properties, making them useful for pH-responsive drug delivery and gene therapy. **Copper oxide (CuO) nanoparticles** exhibit antifungal, antibacterial, and anticancer properties and are often utilized in tumor-targeted drug delivery. Additionally, **hybrid nanoparticles**, such as iron-gold and zinc-iron combinations, integrate the advantages of multiple metals, improving drug delivery efficiency in multimodal imaging and therapy (Sharma et al., 2022). One of the key advantages of metallic nanoparticles is their ability to respond to external stimuli such as pH, light, temperature, and magnetic fields, enabling **stimuli-responsive drug delivery**(Chandrakala et al., 2022). For example, **iron oxide nanoparticles** loaded with **5-fluorouracil (5-FLU)** release the drug in the acidic tumor microenvironment, enhancing therapeutic efficacy. In **tumor-targeted drug delivery**, metallic nanoparticles exploit the **Enhanced Permeability and Retention (EPR) effect**, allowing passive accumulation in cancerous tissues. Functionalized **gold nanoparticles** conjugated with **folic acid** have been effectively used in **breast cancer therapy** to enhance drug specificity. Additionally, metallic nanoparticles show potential in **brain-targeted drug delivery**, overcoming the challenge of the **Blood-Brain Barrier (BBB)**. For instance, **glucose-coated gold nanoparticles** have been used to deliver **lacosamide (LCM)** for epilepsy treatment. These nanoparticles also facilitate the transport of large biomolecules, such as proteins, DNA, and RNA, across cell membranes. **Iron oxide nanoparticles** have been successfully utilized in **gene therapy** for stem cells, further broadening their applications in regenerative medicine and vaccine development (Sharma et al., 2022). Despite their numerous advantages, the use of metallic nanoparticles comes with several limitations. **Toxicity and biocompatibility concerns** arise, particularly with **silver** and **copper oxide nanoparticles**, which may induce oxidative stress and cytotoxicity. The **size and shape of nanoparticles** significantly influence their interactions with biological systems, as smaller nanoparticles can deeply penetrate tissues but may exhibit unpredictable effects. Furthermore, **accumulation and clearance** of nanoparticles from the body pose challenges, as inefficient elimination could lead to long-term toxicity. Additionally, the **high cost and complexity** of synthesizing biocompatible metallic nanoparticles hinder large-scale production. Environmental concerns are another critical issue, as conventional chemical synthesis methods generate hazardous waste. To address this, researchers are exploring **green synthesis approaches**, such as bio-waste-mediated nanoparticle production, to develop eco-friendly and cost-effective alternatives. Overall, metallic nanoparticles have revolutionized drug delivery by enabling controlled and targeted therapy, particularly in cancer treatment, antimicrobial applications, and neurological disorders (kazemi et al., 2023). However, future advancements should focus on reducing toxicity, enhancing biocompatibility, and optimizing large-scale synthesis methods. The integration of **green nanotechnology** holds promise for sustainable and efficient nanoparticle-based drug delivery, paving the way for safer and more effective nanomedicine solutions.

3.3. Pharmacokinetics and Pharmacodynamics of Nanotechnology-Based Drug Delivery System:

Nanotechnology-based drug delivery systems have revolutionized pharmacokinetics and pharmacodynamics by improving drug absorption, bioavailability, controlled release, biodegradability, and clearance mechanisms. These systems are designed to enhance drug absorption by facilitating cellular uptake, particularly for drugs with poor solubility or stability in physiological conditions (Glassman & Muzykantov, 2019). Their nanoscale size enables efficient penetration of biological barriers, leading to improved therapeutic efficacy. Additionally, surface modifications, such as ligand conjugation, allow for receptor-mediated endocytosis, ensuring targeted drug delivery to specific tissues and minimizing off-target effects. Another crucial advantage of nanocarriers is their ability to provide **controlled and sustained drug release**, which prevents fluctuations in plasma drug levels, enhances patient compliance, and reduces systemic toxicity (Adepu & Ramakrishna, 2021b). These delivery systems can also be engineered to respond to specific stimuli, such as pH, temperature, or enzymatic activity, ensuring precise drug release at the desired site and time.

The interaction of nanocarriers with **biological membranes** further enhances drug transport across cellular barriers while protecting encapsulated drugs from premature degradation, ensuring efficient delivery to target sites. Additionally, **biodegradability** plays a crucial role in the safety and efficacy of nanocarriers, as they are designed to break down into non-toxic byproducts post-drug release, preventing accumulation in the body(Y. Liu et al., 2024). The choice of biodegradable materials directly influences drug release profiles and the overall biocompatibility of the delivery system. Furthermore, **clearance pathways** are carefully considered in the design of nanocarriers to ensure their safe elimination from the body, primarily through hepatic (liver) or renal (kidney) pathways, thereby minimizing long-term toxicity risks.

Overall, nanotechnology-based drug delivery systems significantly enhance pharmacokinetics and pharmacodynamics by optimizing drug absorption, ensuring controlled and sustained release, improving interactions with biological membranes, promoting biodegradability, and facilitating safe clearance (Fig. 2). These advancements offer a promising future for targeted and efficient drug delivery, ultimately leading to better therapeutic outcomes and reduced adverse effects in patients (Ezike et al., 2023).

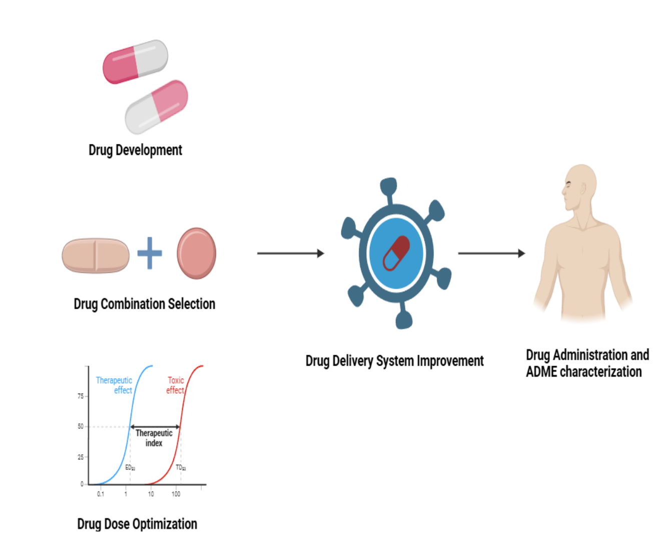

Figure 2. Stages of Drug Development and Delivery

Applications of Nanotechnology-Based Drug Delivery Systems

Nanotechnology-based drug delivery systems (DDS) have revolutionized contemporary medicine by enhancing the effectiveness, precision, and safety of treatments (Fig. 3). These advanced systems offer several key applications across various medical fields (Patra et al., 2018):

(i) **Targeted Drug Delivery**

- Nanoparticles (NPs) can be designed to deliver drugs directly to diseased cells, reducing harm to healthy tissues.
- This is specifically beneficial in cancer therapy, where targeted delivery improves treatment efficacy while minimizing side effects.

(ii) **Cancer Treatment**

- Nanocarriers are widely used in oncology to transport chemotherapeutic agents specifically to tumor sites.
- The enhanced permeability and retention (EPR) effect enables nanoparticles to selectively collect in tumor tissues, improving drug concentration and therapeutic impact (Yao et al., 2020).

(iii) Cardiovascular Diseases (CVDs)

- Nanotechnology aids in delivering cardiac stem cells to damaged heart tissue, facilitating regeneration.
- NPs can also be used for targeted delivery of antihypertensive drugs, improving bioavailability and reducing systemic side effects (Yang et al., 2023).

(iv) Chronic Disease Management

- Nanomedicine enhances treatments for chronic conditions like diabetes and hypertension by ensuring controlled and sustained drug release.
- This reduces the frequency of dosing and improves patient compliance.

(v) Biosensors and Diagnostics

- Nanotechnology is integrated into biosensors for real-time disease detection and monitoring.
- These systems enable early diagnosis, leading to timely interventions and better disease management (Mokhtarzadeh et al., 2017).

(vi) Vaccination and Immunotherapy

- Nanoparticles improve vaccine delivery by enhancing antigen stability and immune response.
- This application is critical in combating emerging infectious diseases and optimizing immunization programs.

(vii) Gene Therapy

- NPs are used to transport genetic material for gene therapy applications.
- This technology has the potential to correct genetic disorders by delivering therapeutic genes directly to target cells.

(viii) Antiviral and Antimicrobial Treatments

- Nanotechnology enhances the effectiveness of antiviral and antimicrobial agents by improving drug stability and bioavailability.
- It is particularly useful in tackling antibiotic-resistant infections.

(ix) Controlled and Sustained Drug Release

- Nanocarriers can be designed for prolonged drug release, maintaining stable plasma levels (Adepu & Ramakrishna, 2021b).
- This controlled mechanism reduces toxicity and enhances treatment efficiency.

(x) Reduction of Adverse Effects

- Encapsulating drugs in nanoparticles minimizes systemic toxicity.
- For example, liposomal formulations of chemotherapy drugs like DOX reduce cardiotoxicity and other side effects.

(xi) Enhanced Drug Stability

- NPs protect drugs from degradation due to environmental factors such as enzymatic activity and pH variations.
- This results in improved drug shelf life and effectiveness (Glassman & Muzykantov, 2019).

(xii) Combination Therapies

- Nanocarriers enable the simultaneous delivery of multiple drugs, improving treatment efficacy.
- This is especially important in cancer therapy and antimicrobial treatments, where drug resistance is a concern.

(xiii) Applications in Neurological Disorders

- NPs can cross the blood-brain barrier, enabling effective treatment of neurological disorders like Alzheimer's and Parkinson's disease (Satapathy et al., 2021).

(xiv) Eye Drug Delivery

- Solid lipid nanoparticles (SLNPs) improve ocular drug delivery, enhancing absorption and therapeutic effects compared to conventional eye drops (Patel et al., 2013).

(xv) Personalized Medicine and Smart Drug Delivery

- Nanotechnology allows for personalized medicine, tailoring drug formulations to individual patients for optimized treatment.
- Smart drug delivery systems can respond to stimuli such as pH, temperature, or enzymes to release drugs precisely where needed (Vora et al., 2023).

➢ **Diseases Benefiting from Nanotechnology-Based Drug Delivery**

Several diseases benefit from nanotechnology applications in drug delivery:

- **Cancer**: Targeted nanoparticle-based therapies improve efficacy and reduce chemotherapy side effects.
- **Cardiovascular Diseases**: Nanoparticles enhance drug delivery for heart disease treatment and tissue regeneration.
- **Infectious Diseases**: Nanotechnology-based antimicrobial agents help combat resistant infections.
- **Neurodegenerative Diseases**: NPs cross the blood-brain barrier, improving treatment for Alzheimer's and Parkinson's.
- **Diabetes**: Nanocarriers optimize insulin delivery,

reducing injection frequency and improving glycemic control.

- **Autoimmune Diseases**: Nanoparticles improve the targeted delivery of immunomodulatory drugs, reducing immune system overactivation.

Nanotechnology-based drug delivery systems have revolutionized modern medicine by providing precise, efficient, and safer treatment options. These advanced systems continue to pave the way for improved therapies across various medical fields, enhancing patient outcomes and advancing healthcare innovation (Y. Liu et al., 2024).

Figure 3. Applications Of Nanotechnology-Based Drug Delivery

Advantages of Drug Delivery Systems

Nanotechnology-mediated drug delivery systems (DDS) have various key benefits that improve the efficacy, safety, and patient compliance of treatments. One of the most critical benefits is **drug targeting**, where nanocarriers can be designed to transport drugs specifically to diseased tissues or cells while reducing contact to healthy tissues. This precision reduces systemic side effects and enhances therapeutic efficacy, particularly in diseases such as cancer (Adepu & Ramakrishna, 2021a). The **enhanced permeability and retention (EPR) effect** further facilitates drug accumulation in tumor tissues, improving bioavailability and treatment outcomes. Additionally, **improved bioavailability** is a key advantage, as nanoparticles enhance the solubility and stability of poorly water-soluble drugs, ensuring a higher concentration reaches systemic circulation for better therapeutic impact.

Another critical feature of nanotechnology-based DDS is **controlled and sustained drug release**, which ensures a gradual and prolonged release of therapeutic agents, maintaining stable plasma drug levels and reducing the need for frequent dosing. This sustained delivery improves patient compliance and minimizes toxicity risks associated with fluctuating drug concentrations. Furthermore, **nanocarriers can overcome biological barriers**, such as the blood-brain barrier, making them effective for treating central nervous system disorders that were previously challenging to address. **Enhanced drug stability** is also a significant benefit, as encapsulating drugs within nanoparticles protects them from degradation due to environmental factors like enzymatic activity and pH fluctuations (Adepu & Ramakrishna, 2021a).

Nanotechnology also enables **combination therapy**, allowing multiple drugs to be co-delivered within a single nanocarrier, which is particularly beneficial in managing multidrug-resistant infections and complex diseases like cancer. Additionally, some nanoparticles exhibit **immunomodulatory effects**, which can be leveraged to enhance immune responses in conditions such as autoimmune diseases (Sultana et al., 2022). The **versatility of nanocarriers** allows for various administration routes, including oral, intravenous, transdermal, and inhalation, providing flexibility in treatment options. Moreover, **biodegradability and clearance pathways** ensure that nanocarriers break down into non-toxic byproducts and are safely eliminated through the liver or kidneys, preventing long-term accumulation in the body.

The future of **personalized medicine** is also greatly influenced by nanotechnology, as nanocarriers can be customized based on individual patient characteristics, improving treatment precision and effectiveness (Fig. 4). Additionally, the potential for **smart drug delivery systems**—where nanoparticles release drugs in response to specific stimuli such as pH, temperature, or enzymes—adds another layer of precision in drug administration (Coelho et al., 2010). Overall, nanotechnology-based drug delivery systems revolutionize modern medicine by enhancing targeted drug delivery, improving bioavailability, enabling controlled release, reducing toxicity, and offering new possibilities for personalized and combination therapies, ultimately leading to safer and more effective treatments.

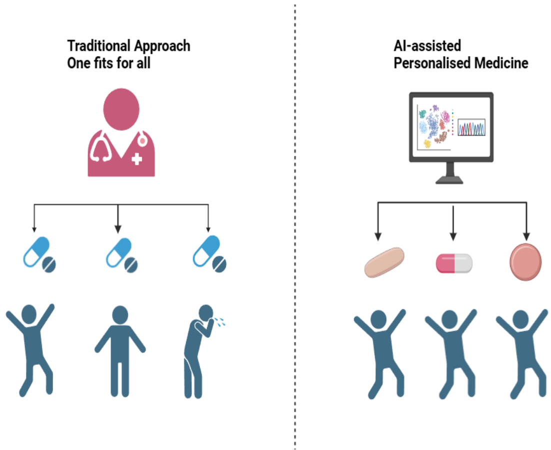

Figure 4: Personalized Medicine

Limitations of Nanotechnology-Based Drug Delivery Systems

Nanotechnology-based drug delivery systems have demonstrated remarkable potential in enhancing therapeutic outcomes; yet their widespread application is impeded by several limitations.

1. **Characterization Challenges**: Characterization of drug-loaded nanocarriers is perhaps one of the greatest challenges. The physicochemical properties of nanoparticles, such as size, shape, surface charge, and drug-loading efficiency, govern their behavior within biological systems. However, existing characterization techniques are not always sufficient to provide precise and reproducible data, leading to inconsistencies in performance and therapeutic efficacy. Robust analytical tools and well-validated protocols are needed to ensure

accurate characterization (Cheng et al., 2023).

2. **Regulatory Hurdles**: The regulatory landscape for nanomedicine is yet to mature, making it difficult to establish universal guidelines for approval. The structural diversity and multifunctionality of nanocarrier systems present a challenge to regulatory bodies, in terms of safety assessments, quality control, and manufacturing standards. The lack of globally accepted protocols for toxicity evaluation and clinical trials results in prolonged approval timelines, slowing down commercialization and clinical adoption.
3. **Safety and Toxicity Concerns**: Although nanocarriers enhance drug targeting and mitigate systemic toxicity, their long-term safety remains a concern. The fate of nanoparticles in the body, including their biodistribution, metabolism, and elimination, needs to be comprehensively investigated to avoid unforeseen toxic effects. Certain nanoparticles may accumulate in organs such as the liver, kidneys, and spleen, leading to potential adverse effects. Further, the immune system may recognize certain nanocarriers as foreign entities, evoking undesirable immune responses. Extensive preclinical and clinical investigations must be conducted to determine their safety profiles (Patra et al., 2018).
4. **Scalability and Manufacturing Issues**: Transitioning nanotechnology-based drug delivery systems from laboratory-scale research to large-scale commercial production is a significant challenge. Batch-to-batch reproducibility and maintenance of the integrity of nanoparticles is difficult owing to variations in synthesis methods, formulation stability, and raw material quality. Advanced manufacturing techniques, such as microfluidics and continuous flow synthesis, are being explored to improve scalability; however, cost-effective large-scale production remains a hurdle (Adepu & Ramakrishna, 2021b).
5. **Stability and Storage Constraints**: The majority of nanocarrier formulations are temperature, humidity, and pH sensitive. Stability during storage and transportation is essential to preserve their therapeutic efficacy. Some nanoparticles tend to aggregate or undergo chemical degradation over time, reducing their effectiveness. Developing robust formulations with enhanced stability and long shelf life is essential for their practical use in clinical settings.
6. **Complexity of Formulations**: The diversity of nanocarriers, including liposomes, dendrimers, polymeric nanoparticles, and metallic nanoparticles, increases the complexity of formulation development. Each one of them has a unique optimization approach to achieve the desired drug release profile, biocompatibility, and targeting efficacy. This complexity increases the time and cost associated with research, development, and regulatory approvals, making widespread adoption more challenging.
7. **Integration of Artificial Intelligence (AI) in Nanomedicine**: AI has the potential to accelerate the nanocarrier design and optimization by predicting their behavior in vivo and designing optimized formulations. However, integrating AI into nanomedicine research is still in its early stages and faces challenges related to data availability, algorithm accuracy, and regulatory acceptance. Establishing reliable AI models that can predict nanoparticle interactions in biological systems requires extensive experimental validation (Coelho et al., 2010).

Addressing these limitations requires a multidisciplinary approach involving researchers, regulatory agencies, and industry stakeholders. Nanofabrication techniques, improved regulatory frameworks, enhanced characterization tools, and innovative stabilization strategies will play a crucial role in overcoming these challenges and realizing the complete therapeutic potential of nanotechnology-based drug delivery systems in clinical practice.

Table 2. Comparative Analysis: Conventional vs. Nanotechnology-Based Drug Delivery Systems

Parameter	Conventional Drug Delivery Systems	Nanotechnology-Based Drug Delivery Systems
Mechanism of Drug Release	Passive diffusion, dissolution, or enzymatic degradation.	Controlled and targeted release using stimuli-responsive nanocarriers.
Targeting Efficiency	Non-specific; drugs are dispersed across the body, resulting in systemic side effects.	High specificity; nanoparticles can be functionalized for active targeting (e.g., ligand-receptor interactions).
Drug Solubility Enhancement	Limited solubility for poorly water-soluble drugs, necessitating solubilizers or chemical modifications.	Nanocarriers enhance solubility and bioavailability without altering the chemical structure of the drug.
Absorption & Bioavailability	Often results in poor bioavailability owing to degradation in the GI tract or first-pass metabolism.	Enhanced bioavailability through improved stability and alternative administration routes (e.g., transdermal, pulmonary).
Controlled Drug Release	Rapid drug release, requiring frequent dosing.	Controlled and sustained release, minimizing dosing frequency and improving patient compliance.

Blood-Brain Barrier (BBB) Penetration	Restricted due to the occurrence of tight junctions hindering drug passage.	Engineered nanoparticles can cross the BBB through receptor-mediated transport, enhancing drug delivery for neurological disorders.
Immunogenicity & Biocompatibility	Increased potential for immune response and toxicity in certain formulations.	Biocompatible nanocarriers decrease immunogenicity and enhance systemic tolerance.
Toxicity & Side Effects	Significant systemic toxicity due to non-specific distribution.	Reduced toxicity through targeted delivery and minimized off-target effects.
Scalability & Manufacturing	Well-established, economically viable large-scale production.	Complex, expensive manufacturing with challenges in reproducibility and batch-to-batch consistency.
Regulatory & Approval Challenges	Standardized regulations exist for most formulations.	Evolving regulatory framework; lack of standardized protocols for safety assessment.
Storage & Stability	Generally stable formulations with long shelf life.	Sensitive to environmental factors (temperature, pH, light), requiring specialized storage conditions.
Cost Implications	Lower development and production costs.	High research, development, and manufacturing costs due to advanced technologies.

Conventional drug delivery methods are cost-effective and well-established but tend to have poor bioavailability, systemic toxicity, and the need for frequent dosing (Sultana et al., 2022). In contrast, nanotechnology-based drug delivery systems offer targeted, controlled drug release, enhanced bioavailability, and reduced side effects (Table 2). However, challenges related to scalability, regulatory approval, and cost need to be addressed before widespread clinical adoption.

Future Scope and Challenges

1. Emerging Trends in Drug Delivery

- **Targeted Drug Delivery**: Surface engineering of nanocarriers facilitates site-specific drug delivery, reducing systemic side effects and improving therapeutic efficacy.
- **Personalized Medicine**: Genetically and disease-profile-based customized treatment regimens enhance efficacy and reduce adverse effects.
- **Long-Acting Drug Delivery:** Sustained-release formulation innovations improve pharmacokinetics, allowing extended drug action with reduced dosing frequency.
- **AI-Driven Drug Delivery Optimization**: Machine learning and predictive modeling aid in optimizing nanocarrier design, stability, and targeting efficiency.
- **Applications in Cancer and Immunotherapy**: Nanocarriers are being investigated for targeted cancer therapies, vaccine development, and immune modulation strategies (Li et al., 2025).
- **Nanotechnology in Vaccine Development**: Nanocarrier-based vaccines for infectious diseases, including COVID-19, are under investigation to enhance immunogenicity and stability.
- **Mobile Health Integration**: Mobile health apps and wearable devices enable real-time monitoring of drug delivery and patient adherence.

2. Research Gaps and Areas for Improvement

- **Understanding of Biological Interactions:** More insights into the behavior of nanocarriers within biological systems, and how to overcome physiological barriers like the blood-brain barrier and the gastrointestinal tract.
- **Standardized Safety and Characterization Protocols**: Existing regulatory measures have no common criteria by which to assess nano-carrier based therapies, resulting in variability in safety evaluations.
- **Stability and Controlled Release**: Instability, aggregation, or premature drug leakage, are the common issues with many nanocarriers, necessitating formulation design enhancements.
- **Scalability and Manufacturing Challenges**: Transitioning from lab-scale synthesis to commercial production is difficult due to challenges in maintaining quality, reproducibility, and cost-efficiency.
- **Integration of AI in Drug Development**: While AI can enhance drug design and optimization, challenges such as interpretability, data reliability, and high computational costs remain (Vora et al., 2023).

3. Challenges in Clinical Translation

- **Toxicity and Safety Concerns**: Potential accumulation of nanoparticles in non-target tissues poses long-term toxicity and biocompatibility concerns.
- **Regulatory and Approval Challenges**: Existing regulatory frameworks face difficulty integrating the novel characteristics of nanomedicines, thus leading to lengthy approval processes (Cheng et al., 2023).
- **Economic and Accessibility Constraints**: High research, manufacturing, and clinical trial costs could

restrict access, especially in low-resource environments.

- **Biodistribution and Long-Term Effects**: Limited research on the metabolism and excretion of nanocarriers hinder their clinical adoption and long-term safety assessment.
- **Complexity of Nanocarriers**: Simplifying nanocarrier structures without compromising functionality is critical for their clinical applicability and patient compliance.

4. Strategies to Overcome Challenges

- **Developing Safer and Biocompatible Nanocarriers**: Research on low-toxicity and biodegradable nanomaterials can improve patient safety (Coelho et al., 2010).
- **Enhancing Large-Scale Production Techniques**: Adopting affordable and reproducible production processes will ensure mass adoption.
- **Regulatory Framework Refinement**: Developing international standards for nanomedicine evaluation will streamline the approval process and provide safety.
- **Advancing AI Integration in Drug Delivery**: Improving AI interpretability and validation in pharmaceutical scenarios will optimize nanocarrier design and drug formulations.
- **Strengthening Biodistribution Studies**: Conducting comprehensive in vivo studies to assess the fate, clearance, and toxicity of nanocarriers is extremely important for clinical translations.

By addressing these challenges through interdisciplinary collaboration, technological innovation, and regulatory improvements, the future of drug delivery systems holds the potential to revolutionize healthcare, improving treatment effectiveness and patient outcomes globally.

CONCLUSION

The development of drug delivery systems from conventional methods to nanotechnology-based approaches has enhanced drug efficacy, stability, and patient compliance. Conventional DDS, although well-rooted and affordable, are faced with shortcomings of poor bioavailability, non-targeted distribution, and frequent dosing requirement. On the other hand, nanotechnology-based drug delivery systems offer enhanced therapeutic benefits through targeted drug delivery, controlled release, enhanced bioavailability, and the ability to cross biological barriers like the blood-brain barrier. Nanocarriers have demonstrated remarkable success in cancer therapy, neurological disorders, cardiovascular treatments, and vaccine formulation. However, the clinical application of these advanced DDS is plagued by challenges which require multidisciplinary collaboration between researchers, industry stakeholders, and regulatory bodies. Future innovations, including AI-driven optimization, biodegradable nanocarriers, and smart drug release mechanisms, hold the potential to revolutionize personalized medicine and change the face of healthcare. With continued research, breaking through current barriers will be crucial to fully harness the potential of nanotechnology in drug delivery, paving the way for safer, more efficient, and accessible therapeutic solutions.

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Ethical Responsibilities of Authors

All authors declare that this research article is original and has not been published elsewhere in any form or language (partially or in full). We declare that this work has not got any financial assistance from funding agency and has not included any study related to humans and/or animals.

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