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## Control Drug Delivery System – Recent Technological Developments

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### ABSTRACT

The abstract presents an overview of advancements in drug delivery systems, focusing on the evolution from conventional methods (like tablets, capsules, and syrups) to more sophisticated controlled delivery approaches. It emphasizes the limitations of traditional drug delivery, including poor bioavailability, inconsistent drug levels in the body, and the inability to sustain therapeutic effects. These shortcomings can make treatments less effective and potentially unsafe. To address these issues, controlled drug delivery systems (CDDS) have been developed, which allow for precise and sustained release of medication at targeted sites. Over the past two decades, these systems have evolved significantly; incorporating innovations at both the macro and nano scales, and now include intelligent systems that can respond to stimuli for targeted drug delivery. Artificial intelligence (AI) has emerged as a powerful tool to revolutionize the healthcare sector, including drug delivery and development. This review explores the current and future applications of AI in the pharmaceutical industry, focusing on drug delivery and development. It provides a comprehensive overview of AI's potential to transform the pharmaceutical industry and improve patient care while identifying further research and development areas. It also covers the fundamental aspects of drug delivery, exploring the pharmacokinetics involved, limitations of conventional methods, and the design and classification of CDDS. It also delves into cutting-edge topics such as nano-drug delivery, targeted therapy, and the use of smart biomaterials, concluding with a discussion of current challenges and future research directions in the field.

**Keywords:** Artificial intelligence, Nano robots, Personalized medicine, Sensor-based devices, Drug discovery, Drug design

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## INTRODUCTION

Controlled drug delivery system (CDDS) is an advanced method of administering therapeutic agents in which the drug is released at a predetermined rate, for a specified period of time, and at a specific target site to achieve optimal therapeutic effect. Unlike conventional dosage forms, such as tablets or injections, that release drugs immediately after administration, controlled drug delivery systems are designed to maintain consistent drug levels in the bloodstream, thereby improving treatment efficacy and patient compliance.

The primary objective of controlled drug delivery is to enhance the safety, effectiveness, and reliability of drug therapy. By regulating the rate and location of drug release, these systems minimize fluctuations in plasma drug concentration, reduce dosing frequency, and lower the risk of side effects and toxicity. This approach is particularly beneficial for drugs with short half-lives, narrow therapeutic indices, or those requiring long-term administration.

Controlled drug delivery systems utilize various technologies and carriers, including polymers, hydrogels, nanoparticles, liposomes, and transdermal patches, to achieve sustained, targeted, or stimuli-responsive drug release. Advances in material science, biotechnology, and nanotechnology have further expanded the scope of CDDS, enabling site-specific delivery and personalized medicine.



**Figure 1: Dosage Form**

Overall, controlled drug delivery systems represent a significant advancement in pharmaceutical sciences, offering improved therapeutic outcomes, better patient adherence, and enhanced quality of life compared to conventional drug delivery methods. <sup>(1,2)</sup>

Controlled drug delivery systems can include the maintenance of drug levels within a desired range, the need for fewer administrations, optimal use of the drug in question, and increased patient compliance. While these advantages can be significant, the potential disadvantages cannot be ignored like the possible toxicity or non-biocompatibility of the materials used, undesirable by-products of degradation, any surgery required to implant or implant or remove the system, the

chance of patient discomfort from the delivery device, and the higher cost of controlled-release systems compared with traditional pharmaceutical formulations.

The ideal drug delivery system should be inert, biocompatible, mechanically strong, comfortable for the patient, capable of achieving high drug loading, safe from accidental release, simple to administer and remove, and easy to fabricate and sterilize. The goal of many of the original controlled-release systems was to achieve a delivery profile that would yield a high blood level of the drug over a long period of time. With traditional drug delivery systems, the drug level in the blood follows the in which the level rises after each administration of the drug and then decreases until the next administration.

The key point with traditional drug administration is that the blood level of the agent should remain between a maximum value, which may represent a toxic level, and a minimum value, below which the drug is no longer effective.

Drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect on disease. Conventional dosages mean oral delivery and injection are the predominant routes for drug administration. The main drawbacks of these types of dosage are non-local treatment and toxicity to healthy tissues. An ideal drug delivery would be controlled for high efficiency treatment and local drug release to minimize toxicity. With the development of micro/nano drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect on disease. Conventional dosages mean oral delivery and injection are the predominant routes for drug administration. The main drawbacks of these types of dosage are non-local treatment and toxicity to healthy tissues. An ideal drug delivery would be controlled for high efficiency treatment and local drug release to minimize toxicity. With the development of micro/nano electromechanical system (MEMS/NEMS) technology and material science, a variety of devices have been developed to achieve drug delivery for disease treatment over the years. The devices with micro/nanostructures, as powerful platforms, can provide better drug therapy because they allow precise, local, and controlled dosing with lower toxicity. These devices can offer opportunities to address unmet medical needs related to disease therapy.<sup>(3, 4)</sup>

An ideally controlled drug delivery system requires simultaneous consideration of several factors, such as the mechanism of drug release, the route of administration, and capability of targeting. The approach of drug release has a significant effect on therapeutic efficacy. An ideal approach should maintain drug levels within the therapeutic window to avoid potential health hazards, maximize therapeutic efficiency, and provide a well-controlled drug release triggered by stimuli. Drug concentration above the therapeutic window is toxic, and below the therapeutic window will lose

therapeutic efficacy. Conventional drug delivery systems, such as oral and injection, generally have a high initial level of the drug after the first administration, followed by sharp decrease in blood concentration. Controlled drug release helps to address this issue, shows two profiles of most common time dependent release, sustained release, and pulsatile release. Sustained release can offer a constant drug concentration within the therapeutic window. However, pulsatile release provides a consecutive burst drug delivery.

To improve treatment efficiency of the disease, controlled drug delivery can be achieved in different approaches based on different compounds or different therapeutic needs. Most treatments request a sustained release of drug at a constant rate over long periods of time. For some specific drugs, such as insulin and hormones, the drug release should mimic the body's natural pulsatile. A variety of controlled drug delivery devices have been developed to achieve a good therapeutic effect over the years. Controlled drug release can be triggered by different stimuli, such as temperature, pH, magnetic and electric field, etc. These devices use different routes of administration, and different methods and materials for device fabrication, typically including polymer- and silicon-based micropumps, microneedles, microreservoirs, and microfluidic systems. (5, 6)

### **SIGNIFICANCE OF CDDS**

Controlled drug delivery systems (CDDS) are required to overcome the critical limitations of conventional medications, such as standard tablets or injections, which often cause rapid fluctuations in drug levels and require frequent dosing. By regulating the release rate, these systems ensure a more stable, safe, and effective therapeutic experience. (7, 8, 9)

The primary requirements for these systems include:

#### **Maintaining the Therapeutic Window**

Conventional drugs often create "peaks" (potentially toxic) and "troughs" (ineffective) in the bloodstream. CDDS maintain a constant drug concentration within the therapeutic window—the range where the drug is effective without being harmful. Many systems aim for a zero-order release profile, where the drug is released at a constant rate over time, independent of its remaining concentration.

#### **Improving Patient Compliance and Safety**

Because the drug is released slowly over hours, days, or even months, patients do not need to take multiple daily doses, which is especially vital for chronic conditions like diabetes or hypertension. By avoiding high initial concentration "spikes," CDDS reduce the risk of systemic or local adverse

effects. These systems can protect delicate molecules (like proteins or peptides) from being degraded by stomach acid or enzymes before they reach their target.

### **Precision and Targeted Delivery**

CDDS can be engineered to release medication only at a specific site (e.g., a tumor or inflamed joint), which increases efficacy at the diseased area while sparing healthy tissues from exposure. Advanced "smart" systems can be triggered to release a drug in response to specific environmental changes, such as pH, temperature, or the presence of specific enzymes.

### **Overcoming Biological and Chemical Barriers**

For drugs with a very short biological half-life, CDDS provide a continuous supply to keep them active in the body longer. They can improve the absorption of poorly soluble drugs by keeping the tract.

Some other significant points of CDDS are –

1. Help in early identification of developmental delays in children
2. Enable early intervention, which improves long-term outcomes
3. Prevent permanent disability and reduce severity of impairments
4. Support normal growth and development of the child
5. Guide parents and caregivers for timely referral and management
6. Reduce emotional, social, and economic burden on families
7. Improve school readiness and learning abilities
8. Assist health workers in planning child health services
9. Contribute to better quality of life for affected children

### **APPLICATIONS** <sup>(10, 11)</sup>

#### **Chronic Disease Management**

Diabetes: Insulin pumps and controlled release insulin formulations are used to maintain steady blood glucose levels, minimizing the need for frequent injections. - Example: Continuous subcutaneous insulin infusion (CSII) via insulin pumps. - Hypertension: Controlled-release formulations of antihypertensive drugs (e.g., calcium channel blockers, beta blockers) help maintain stable blood pressure over 24 hours with once-daily dosing.

Example: Sustained-release forms of amlodipine or metoprolol.

#### **Cancer Therapy**

Targeted Drug Delivery: CDDS such as nanoparticles, liposomes, and antibody drug conjugates are used to deliver chemotherapeutic agents directly to tumors, reducing systemic toxicity. - Example: Liposomal doxorubicin (Doxil) for the treatment of ovarian cancer and Kaposi's

sarcoma. - Localized Drug Delivery: Implants or injectables can release chemotherapeutic agents directly into or near the tumor site, providing high local concentrations with minimal systemic exposure. - Example: Gliadel wafer (carmustine implant) for the treatment of brain tumors.

### **Pain Management**

Sustained-Release Analgesics: CDDS provide prolonged relief from chronic pain conditions, such as cancer pain, neuropathic pain, or post-surgical pain, reducing the frequency of administration and minimizing fluctuations in plasma levels. - Example: Fentanyl transdermal patches for chronic pain management. - Localized Pain Relief: Drug delivery systems like injectable depots or intra articular injections deliver anesthetics or analgesics directly to the site of pain. - Example: Injectable bupivacaine liposome suspension (Exparel) for post-operative pain relief.

### **Hormone Replacement Therapy (HRT)**

Transdermal Patches: Controlled release hormone patches deliver hormones (e.g., estrogen, progesterone) steadily over time, ensuring stable plasma levels and reducing the risk of side effects associated with hormone fluctuations.

Example: Estradiol transdermal system for hormone replacement in menopause. - Implants: Hormone-releasing implants, such as those used for contraception or testosterone replacement therapy, provide long-term drug release over months or years. - Example: Etonogestrel implant (Nexplanon) for contraception.

### **Neurological Disorders**

Parkinson's disease: Controlled-release formulations of levodopa or dopamine agonists maintain more stable dopamine levels in the brain, reducing motor fluctuations and improving symptom control. - Example: Extended-release carbidopa levodopa (Rytary). - Epilepsy: Sustained-release formulations of anticonvulsants (e.g., lamotrigine, valproic acid) are used to maintain steady therapeutic levels and reduce seizure frequency. - Example: Lamotrigine extended release for epilepsy.

### **Infectious Disease Treatment**

Antibiotics: Controlled-release formulations of antibiotics ensure prolonged exposure to the pathogen, improving treatment efficacy and reducing the need for frequent dosing. - Example: Liposomal amphotericin B (Ambisome) for fungal infections. - Antiretrovirals for HIV: Long-acting injectables and sustained-release formulations of antiretrovirals ensure steady drug concentrations, improving adherence and reducing viral replication. - Example: Cabotegravir long-acting injectable (Cabenuva) for HIV treatment.

### **Cardiovascular Disease**

Sustained-Release Cardiovascular Drugs: Controlled-release formulations of drugs like beta-blockers, calcium channel blockers, and antiplatelet agents provide consistent therapeutic effects, reducing the need for frequent dosing. - Example: Metoprolol succinate extended-release for heart failure and hypertension. - Drug-Eluting Stents: Stents coated with drugs (e.g., paclitaxel, sirolimus) are implanted in coronary arteries to release drugs that prevent restenosis (re-narrowing) of the arteries. - Example: Sirolimus-eluting coronary stents.

### **Contraception**

Implants and Injections: Hormonal implants (e.g., etonogestrel) or injections (e.g., depot medroxyprogesterone acetate) release contraceptive hormones slowly over several months or years, providing long term contraception. - Example: Depo-Provera (depot medroxyprogesterone acetate) injection. - Intrauterine Devices (IUDs): Hormone releasing IUDs deliver levonorgestrel continuously for several years, providing long-term birth control. - Example: Levonorgestrel-releasing intrauterine system (Mirena).

### **Respiratory Diseases**

Inhalation-Based Controlled Delivery: Inhalation systems, such as metered-dose inhalers (MDIs) or dry powder inhalers (DPIs), deliver bronchodilators or corticosteroids in a controlled manner to the lungs, helping manage conditions like asthma and chronic obstructive pulmonary disease (COPD). - Example: Fluticasone/salmeterol inhalation (Advair) for asthma.

Pulmonary Drug Delivery for Systemic Effect: Controlled-release formulations of drugs like insulin or antibiotics can be delivered via the lungs for systemic absorption. - Example: Inhaled insulin (Afrezza).

### **Ocular Drug Delivery**

Intraocular Implants: Controlled-release implants are placed inside the eye to deliver drugs for treating chronic ocular conditions like glaucoma, macular degeneration, or uveitis. - Example: Fluocinolone acetonide implant (Retisert) for chronic uveitis. - Eye Drops with Sustained Release: Certain formulations allow for prolonged drug action, reducing the need for frequent administration in treating conditions like dry eye or glaucoma. - Example: Timolol maleate extended release eye drops for glaucoma.

## **NEW TECHNOLOGICAL DEVELOPMENTS IN CDDS**

Technology plays a pivotal role in the design, function, and advancement of Controlled Drug Delivery Systems (CDDS), enabling precise, targeted, and on-demand therapeutic administration that was previously impossible with conventional methods. These technological applications span from the materials used to create the delivery systems to the integration of microelectronics and

artificial intelligence for enhanced control and personalized medicine. Some new technologies used in CDDS include:

### **ADVANCED MATERIALS AND NANOTECHNOLOGY**

The foundation of most CDDS is advanced materials, primarily polymers (both natural and synthetic), lipids, and ceramics, which can be engineered to control drug release kinetics.

#### **Polymers:**

These materials are integral to systems like matrix tablets, reservoir devices, and hydrogels. Their properties (biodegradability, swelling capacity, pH sensitivity) are precisely engineered to manage how a drug is released over time via diffusion, dissolution, or erosion mechanisms.

#### **Nanoparticles and Liposomes:**

Nanotechnology allows for the creation of carriers (e.g., liposomes, polymeric nanoparticles, nanoemulsions, mesoporous silica) that can encapsulate drugs and target specific tissues or cells (such as cancer cells), thereby increasing efficacy and minimizing systemic toxicity.

#### **"Smart" or Stimuli-Responsive Materials:**

These advanced materials are designed to respond to specific internal or external triggers, such as changes in pH, temperature, enzyme activity, or light. This allows for the "on-demand" or "site-specific" release of drugs, highly beneficial for conditions like cancer where the tumor microenvironment has a different pH than healthy tissue.

#### **Micro fabrication and Biomedical Devices**

Miniaturization technologies allow for the creation of sophisticated, implantable devices that offer unparalleled control over drug administration.

#### **Microelectro mechanical Systems (MEMS):**

MEMS technology is used to fabricate miniature devices, including micropumps, microreservoirs, and microfluidic channels, on a tiny chip. These devices can store and release drugs with high precision, often controlled by actuators that respond to electric fields or pressure.

#### **Implantable Devices:**

These micro-devices can be implanted in the body (e.g., in the eye for glaucoma, or subcutaneously for hormone delivery) to provide consistent drug levels over weeks, months, or even years, eliminating the need for frequent administration.

#### **Microneedle Patches:**

These patches use arrays of microscopic needles to painlessly deliver drugs, including large molecule biologics, through the skin as an alternative to injections.

### **ADVANCED MANUFACTURING AND DIGITAL INTEGRATION**

Modern manufacturing techniques enhance the customization and efficiency of CDDS production.

### **3D Printing:**

This technology is transforming drug formulation by enabling the fabrication of complex, personalized dosage forms with specific shapes, sizes, and internal structures to achieve unique or multi-phase drug release profiles tailored to an individual patient's needs.

### **Intelligence (AI) and Machine Learning:**

AI is increasingly used in the design, optimization, and development of new CDDS. It helps in predicting optimal drug-excipient combinations, designing Artificial nanocarriers for targeted delivery, and personalizing treatment regimens by analyzing

### **Connectivity and Monitoring:**

"Smart" devices, such as connected inhalers or electronic pill bottles with sensors, monitor patient adherence and wirelessly transmit data to healthcare providers, allowing for real-time monitoring and adjustment of treatment plans.

### **Electronic Monitoring:**

Smart pillboxes, electronic pill bottles (e.g., Glow Cap), and ingestible sensors that track when a dose is taken.

### **Wearable Sensors:**

Wrist-worn devices that use motion sensors to detect medication-taking behavior.

## **ARTIFICIAL INTELLIGENCE (AI) IN CDDS**

Artificial intelligence (AI) is transforming Clinical Decision Support Systems (CDSS) by enhancing efficiency, accuracy, and personalization in healthcare delivery. It moves beyond traditional support systems to provide more proactive, data-driven insights across various aspects of patient care and pharmaceutical practice.

## **IMPORTANCE OF AI IN CDSS**

### **Enhanced Diagnostic Accuracy:**

AI algorithms can analyze vast datasets, including medical imaging (X-rays, CT scans, MRIs, pathology slides), lab results, and clinical notes, to detect diseases at earlier stages and with greater accuracy than traditional methods. This aids clinicians in making more informed and timely diagnoses.

### **Personalized Medicine and Treatment Plans:**

AI enables the creation of tailored treatment regimens based on an individual patient's unique genetic profile, medical history, and lifestyle factors. By predicting how a patient might respond to

specific drugs, AI helps optimize dosages and minimize adverse effects, moving away from a "one-size-fits-all" approach.

#### **Improved Drug Safety and Pharmacovigilance:**

AI significantly enhances the monitoring of drug safety after a product is on the market. It can rapidly analyze large amounts of real-world data, including electronic health records (EHRs) and social media, to detect potential adverse drug reactions (ADRs) and safety signals much faster than manual review.

#### **Reduced Medication Errors:**

AI-powered systems within pharmacies and hospitals help verify prescriptions, check for potential drug-drug interactions, and suggest alternative medications in cases of allergies or contraindications, thereby minimizing human error in medication management.

#### **Optimized Clinical Workflows:**

AI automates repetitive administrative tasks, such as data entry, documentation, and information retrieval, freeing up healthcare professionals to focus on more complex patient care activities.

#### **Formulation Design:**

AI algorithms analyze drug/excipient interactions to suggest optimal carriers (nanoparticles, hydrogels) for better solubility, stability, and release profiles, notes Cureus and Lippincott.

#### **Personalized Treatment:**

AI integrates genetic, lifestyle, and disease data to tailor drug release, dosage, and timing for individual patients, improving outcomes and reducing side effects, say National Institutes of Health (NIH) and RSC Publishing.

#### **Smart Nanorobots:**

AI powers autonomous nanorobots with sensors and microchips to navigate, target specific cells (e.g., based on pH), and release drugs precisely, improving efficacy and minimizing harm, writes YMER.

#### **Predictive Modeling:**

Machine learning models predict drug release kinetics, therapeutic responses, and potential toxicity, optimizing system performance before physical testing, according to Science Direct and National Institutes of Health (NIH).

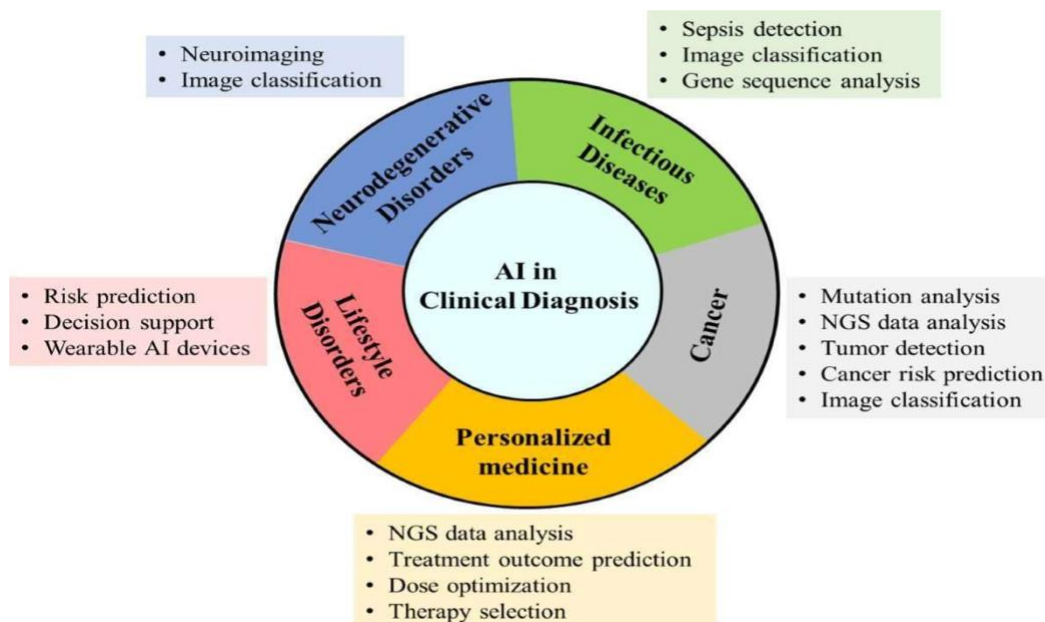
#### **Quality & Manufacturing:**

AI monitors production, analyzing sensor data to ensure consistency and detect defects in tablets and other delivery systems, mentions International Journal for Multidisciplinary Research

(IJFMR).

### Bio-mimicry:

AI, like Artificial Neural Networks (ANNs), simulates biological processes to create sophisticated



control algorithms for drug delivery, note International Journal of Technology (IJT) and Science Direct.

**Figure 2: AI in Clinical Diagnosis**

- Hydrogel systems for controlled insulin release.
- AI-designed nanocarriers for targeted cancer therapy.
- Supports early diagnosis and disease prediction
- Assists healthcare professionals in evidence-based decision-making
- Reduces medical errors and improves patient safety
- Enables personalized treatment plans based on patient data
- Processes real-time clinical information for timely interventions
- Enhances accuracy of clinical decisions by analyzing large and complex datasets

### Challenges and future direction <sup>(12, 13)</sup>

Systems for administering controlled medications have advanced significantly over the last 20 years. Development is still required to get past the constraints and broaden possible futures.

### Microfluidics in controlled drug delivery

It seems promising that controlled and implanted microfluidic delivery devices will be the main focus of future studies. Lab-on-a-chip (LOC) technology is commonly used because it uses small micro devices containing chambers and channels. <sup>(14)</sup> The fluid flow behaviour is controlled by

these tiny devices to better deliver the drug to the intended site.<sup>(15)</sup> Recent studies have proposed polymerizing  $\alpha$ -amino acid N-carboxy anhydrides (NCAs) to create synthetic polypeptides that can be shaped into nanostructures and deliver the drug exactly to a specific location. Altering the polypeptide structure's chemical and physical characteristics can also control the release of medicinal drugs.<sup>(16)</sup>

### **Intelligent Biomaterials**

There is a lot of promise for intelligent biomaterials that can sense their environment, adapt to it on their own, and regulate the release of drugs. For example, an intelligent hydrogel may sense the pH or temperature of its immediate environment to determine the blood sugar levels in that environment. The precise amount of insulin needed to sustain such levels would then be provided. Since smaller biosensor hydrogels are more delicate and cannot be given the mechanical strength to carry out the necessary function, it is currently difficult to build smaller hydrogels, despite the fact that doing so is important.<sup>(17)</sup>

### **Nano medicine improvements and challenges**

The ability of nanoparticles to cross the blood-brain barrier is beneficial in brain diseases, but it also causes neurotoxicity when the intended site of action is not the brain. Nanoparticles can sometimes have immunomodulatory effects as well. Using this of nanoparticles, inflammatory monocytes can be targeted across the blood-brain barrier to inhibit the progression of auto-immune illnesses encephalomyelitis. One of the many benefits of using nano-drug delivery systems instead of more conventional ones is the ability to administer drugs more effectively and more efficiently. However, toxicology and safety characteristics for nano-particulate systems need to be mesoporous nanoparticles have sparked interest in regulated drug administration. For better drug targeting and endosomal release, they are hence ideal. To prevent the early release of pharmaceuticals through mesopores, stimuli responsive polymers can be used to line them and give spatiotemporal control during the release of a particular medicament into the cytoplasm of the target cell.<sup>(18)</sup>

### **CONCLUSION:**

Controlled drug delivery systems (CDDS) represent a significant advancement in modern therapeutics, offering precise, sustained, and targeted drug release that improves treatment efficacy and patient compliance. They have revolutionized the management of chronic diseases, cancer therapy, pain relief, and many other conditions. Despite their numerous advantages, challenges remain, such as manufacturing complexities, regulatory hurdles, patient variability, and ensuring biocompatibility and safety. The future of CDDS is promising, with advances in nanotechnology,

smart materials, personalized medicine, and gene therapy poised to overcome current limitations. The integration of AI, bioinformatics, and bioinspired designs will further enhance the precision and adaptability of these systems. Ultimately, the development of more sophisticated, cost-effective, and patient-friendly drug delivery solutions will continue to transform healthcare, offering more effective treatments while minimizing side effects and improving overall patient outcomes.

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