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Advances, Obstacles, and Emerging Horizons in Controlled Drug Delivery: A Comprehensive Review

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Abstract: Controlled drug delivery (CDD) is a specialized pharmaceutical strategy in which engineered carrier systems are employed to modulate the speed, timing, and anatomical site of drug release within the body.

Conventional immediate-release formulations frequently fall short due to inadequate bioavailability, imprecise targeting, and poor patient adherence. In contrast, CDD platforms are designed to sustain drug concentrations within the therapeutic window over prolonged intervals, thereby curtailing the plasma fluctuations that otherwise precipitate either toxicity or subtherapeutic outcomes. Among their chief advantages are the reduction of dosing frequency and the promotion of patient adherence, particularly in the long-term management of chronic illnesses.

This article surveys recent progress in CDD, focusing on three major technological frontiers: (i) nanotechnology-based CDD, which harnesses nanocarriers such as liposomes and polymeric nanoparticles for site-selective cancer targeting via passive and active mechanisms; (ii) stimuli-responsive drug delivery systems (SRDDS), which are engineered to release their therapeutic payload in response to biological or physicochemical cues including pH shifts, thermal gradients, and redox states; and (iii) targeted drug delivery strategies, including novel approaches that exploit the endocannabinoid system. Advanced fabrication methods such as microfluidics and electrospinning have further propelled the field by enabling more reproducible, uniform drug carriers.

Notwithstanding this considerable progress, several obstacles continue to impede broader clinical adoption. These encompass navigating intrinsic biological barriers such as the blood-brain barrier and mucosal interfaces, resolving safety and toxicity concerns around biomaterial compatibility and erratic release kinetics, and closing the clinical translation gap that persists due to overly simplified preclinical models and complex scale-up requirements.

Prospectively, CDD is well-positioned to underpin personalised and precision medicine, enabling treatment regimens calibrated to individual genomic profiles. The discipline will be further transformed by the incorporation of Artificial Intelligence and Machine Learning, which promise to accelerate formulation optimization and strengthen predictive modelling.

Keywords: *Controlled Drug Delivery, Sustained Release, Bioavailability, Patient Compliance, Targeted Delivery, Polymers, Liposomes, Nanoparticles, Biodegradable Materials, Diffusion, Degradation, Stimuli-Responsive Systems, Nanotechnology, Microfluidics, Electrospinning, Artificial Intelligence, Machine Learning, Cancer Therapy, Personalized Medicine, Passive Targeting, Active Targeting, Biological Barriers, Blood-Brain Barrier, Toxicity, Biocompatibility, Clinical Translation, Regulatory Challenges, Smart Drug Delivery Systems.*

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I. INTRODUCTION

The fundamental goal of any drug delivery system is the efficient transport of pharmacologically active compounds to their sites of action, generating a predictable and reproducible therapeutic effect. Despite decades of pharmaceutical advancement, conventional delivery modalities still face critical shortcomings: suboptimal drug bioavailability, unpredictable and fluctuating plasma concentrations, and an inability to maintain prolonged drug action. These

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deficiencies can compromise treatment efficacy and ultimately diminish patient outcomes.

A. Background and Importance of Drug Delivery Systems:

From a pharmacological standpoint, controlled drug delivery encompasses a class of formulation technologies specifically devised to govern the rate, duration, and anatomical site of drug release. Unlike standard immediate-release products, these platforms are built to sustain therapeutic concentrations across extended time frames, actively reducing the peaks and troughs in plasma levels that contribute to toxic episodes or inadequate therapeutic coverage (1).

Traditional drug delivery platforms carry several well-documented limitations that negatively affect clinical outcomes. In the oral route, poor aqueous solubility and restricted loading capacity constrain bioavailability, often mandating higher doses and elevating adverse effect risks (2). Ocular formulations present a distinct challenge: eye drops and ointments suffer from rapid nasolacrimal drainage and minimal corneal contact time, both of which drastically curtail the fraction of drug reaching the target tissues and diminish patient adherence (3). These anatomical constraints are compounded by the eye's physiological barriers, further restricting absorption. Beyond route-specific challenges, most conventional systems lack the resolution to direct therapeutic agents to defined cellular or tissue targets, resulting in off-target distribution, systemic toxicity, and diminished therapeutic index (4). CDD platforms have emerged specifically to overcome these shortcomings through precise dosing control and sustained release profiles, thereby reducing adverse effects while improving clinical benefit (5,6). Yet, advancing from conventional to CDD-based approaches demands rigorous safety testing and quality assurance protocols to verify both efficacy and patient protection (6). In summary, the evolution from conventional to controlled systems represents a necessary step toward more bioavailable, targetable, and patient-compliant pharmacotherapy (9,11).

Relative to standard formulations, CDD systems confer multiple therapeutic advantages. Their capacity to maintain plasma drug concentrations within the therapeutic range reduces the dosing burden and associated side effects (7,8). Predetermined release kinetics facilitate consistent drug exposure, an essential feature when managing conditions that demand stable therapeutic levels such as epilepsy, diabetes, or cardiovascular disease (7,9). The incorporation of advanced carrier materials—polymers, liposomes, and nanoparticles—provides an additional dimension of control, protecting the drug from premature degradation while permitting tunable release characteristics (7,10). These materials also support improved tissue targeting and the traversal of physiological obstacles such as the blood-brain barrier, lowering systemic exposure and potential toxicity (10). The addition of stimuli-responsive ligands enables further site-specific precision, maximizing drug utility at the target while sparing non-target tissues (7,11). Although biocompatibility challenges and higher manufacturing costs remain practical concerns, continued innovation in materials science and formulation engineering is progressively overcoming these barriers, positioning CDD as a cornerstone of future therapeutic design (9,11).

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B. Scope and Objectives of the Review:

This review aims to deliver a systematic appraisal of the current state of CDD—surveying recent technological breakthroughs, identifying the principal clinical and biological obstacles, and delineating emerging directions. Particular attention is given to innovations in nanotechnology and stimuli-responsive platforms, together with the biological and regulatory challenges that must be surmounted before these technologies achieve their full clinical potential.

II. FUNDAMENTAL CONCEPTS AND MECHANISMS OF CONTROLLED DRUG DELIVERY

Achieving a well-defined drug release profile from a CDD system requires the integrated design of multiple functional components. A critical element in many formulations is the controlled-release layer, a membrane or matrix that dissolves or erodes at a predetermined rate upon contact with physiological fluids, releasing drug in a sustained fashion. Supplementary regulatory mechanisms—including check valves, magnetic actuation units, and multi-layer electromagnetic coils—allow dynamic modulation of release kinetics, as has been demonstrated in gastrointestinal delivery platforms (12). The sensitivity of stimuli-responsive polymers to physiological parameters such as pH and temperature further enhances the adaptability of these systems to the local disease environment (7,10). Nanotechnology-derived carriers, including liposomes and polymeric micelles, extend these capabilities by enhancing drug solubilization, enabling targeted delivery, and reducing non-specific toxicity (5,10).

Collectively, these design elements work in concert to yield drug delivery that is both therapeutically effective and aligned with patient-centric treatment goals.

A. Materials Used in CDD:

Biodegradable polymers dominate the landscape of CDD carrier materials. Among the most widely adopted are poly(lactic acid) (PLA), poly(lactide-co-glycolide) (PLGA), polycaprolactone (PCL), chitosan, and gelatin—each selected for its established safety profile, capacity to encapsulate diverse drug classes, and highly tunable degradation kinetics spanning hours to several weeks (13,14). PLGA has achieved particular prominence in parenteral depot formulations, where its degradation rate can be precisely modulated to yield sustained, therapeutically relevant plasma concentrations with minimal dosing frequency (13). Drug release from these carriers proceeds through multiple mechanisms—diffusion through the polymer matrix, dissolution of the carrier itself, and hydrolytic or enzymatic degradation—which can be independently engineered to target specific release profiles and tissue sites (15). Nanocomposites derived from these biodegradable polymers further augment performance by improving the aqueous solubility and overall bioavailability of poorly water-soluble drugs (16).

III. RECENT ADVANCES IN CONTROLLED DRUG DELIVERY SYSTEMS

The following section examines landmark innovations within CDD and their contributions to overcoming the recognized deficiencies of conventional formulations.

A. Nanotechnology-Based CDD:

Nanotechnology has catalyzed a new generation of CDD solutions with particular impact in oncology. Nanocarriers—including liposomes, dendrimers, and polymer-based nanoparticles—exploit both passive accumulation (via the enhanced permeability and retention effect) and ligand-driven active targeting to concentrate therapeutic agents within solid tumors while protecting healthy tissue from drug-related injury (17,18). The development of stimuli-responsive nanoparticles, engineered to discharge their payload specifically in response to tumor microenvironmental signals, further refines treatment selectivity (19). The ability to co-load synergistic drug combinations within a single nanocarrier also offers a promising avenue for countering mechanisms of drug resistance (20). Despite these advances, significant challenges remain unresolved, particularly those relating to manufacturing scalability, prolonged biocompatibility, and the navigating complex regulatory requirements for novel nanomedicines (21). Sustained interdisciplinary research bridging materials science, pharmacology, and clinical medicine will be essential for translating these nanotechnological innovations into routine oncological care (18,19).

B. Stimuli-Responsive Drug Delivery Systems:

SRDDS constitute a major advance in precision pharmacotherapy, providing dynamic, on-demand drug release that is governed by the pathological milieu rather than a fixed schedule. By linking therapeutic release to measurable disease signals, SRDDS can achieve a degree of individualization that conventional systems cannot match. The principal categories and their clinical applications are outlined below.

➢ *Types of Stimuli-Responsive Drug Delivery Systems:*

- pH-responsive: Drug release is triggered by acidic or alkaline environments characteristic of tumors or inflamed mucosal tissue, enabling selective targeting of pathological sites where pH deviates from physiological norms (22).
- Temperature-responsive: These platforms exploit localized hyperthermia—whether pathological or externally induced—as a trigger, releasing drug payload preferentially in heated tissue regions (23).
- Photo-Sensitive: Light-activated carriers respond to specific optical wavelengths, affording spatiotemporal control over drug release through non-invasive external stimulation (24).
- Redox-responsive: Elevated glutathione concentrations and other reductive conditions prevalent in the tumor interior are harnessed to initiate drug discharge selectively within malignant tissue (25).

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- Biological Stimuli: Systems programmed to detect disease-specific biochemical signals—such as overexpressed enzymes or glycemic fluctuations—are especially valuable for diabetes management and enzyme-targeted cancer therapy (26).

➢ *Applications in Modern Medicine:*

- Cancer Treatment: Clinical and preclinical evidence suggests SRDDS can markedly improve tumor response, with selected studies reporting efficacy gains in the region of 37% over conventional chemotherapy (24).
- Diabetes Management: Glucose-sensing insulin delivery systems have demonstrated reductions in hypoglycaemic episodes of up to 42% in controlled settings, representing a meaningful safety improvement (24).
- Inflammatory Diseases: pH- and enzyme-responsive carriers have shown clinically significant improvements in endoscopic remission rates in inflammatory bowel disease, underscoring their translational potential (24).
- Personalised Medicine: The inherent programmability of SRDDS makes them natural candidates for individualized treatment strategies, directly addressing the one-size-fits-all limitations of standard pharmacotherapy (25).

While SRDDS hold considerable promise, large-scale production and regulatory validation remain significant bottlenecks. Continued investment in process development and standardized testing frameworks will be necessary to realize their full therapeutic impact.

C. Targeted Drug Delivery Strategies:

Contemporary targeted delivery strategies integrate nanotechnological, cellular, and receptor-based approaches to achieve unprecedented specificity. In cancer therapy, nanocarriers are engineered to accumulate preferentially at tumor sites by exploiting leaky vasculature (passive targeting) or by surface-decorating carriers with ligands that bind to receptors overexpressed on malignant cells (active targeting), thereby concentrating drug at the intended site while restricting systemic exposure (27,28). Microenvironmental responsiveness—triggered by tumor-associated pH, enzymatic activity, or temperature—grants an additional layer of selectivity (28). The endocannabinoid system (ECS) represents an emerging and underexplored targeting paradigm: a thorough understanding of its receptor pharmacology and downstream signaling networks may enable the rational design of cannabinoid-loaded nanocarriers with precisely defined tissue selectivity (29). Cell-based delivery vehicles—where patient-derived immune cells or erythrocytes are loaded with therapeutic agents—represent yet another strategy for achieving tissue specificity through the natural trafficking behavior of biological cells (30). Both passive and active targeting modalities are frequently combined to maximize precision, although issues of nanocarrier opsonization and consequent immunological clearance, as well as residual carrier toxicity, continue to be active areas of investigation (27,28).

Taken together, these targeting strategies offer substantive prospects for improving disease-specific treatment outcomes while limiting collateral damage to healthy tissues.

D. Advanced Manufacturing Techniques:

Microfluidics and electrospinning have emerged as transformative fabrication tools for next-generation drug delivery platforms. Microfluidics enables exquisitely fine control over fluid dynamics at the microscale, facilitating the reproducible synthesis of nanocarriers with defined particle size distributions and shapes—properties that are critical determinants of in vivo pharmacokinetic behavior (32,33). The technology directly addresses the inefficiency and batch variability inherent to conventional bulk-mixing approaches, supporting rapid, scalable production of sustained-release formulations (34,35). Electrospinning, meanwhile, generates ultrafine fibrous scaffolds and nano/microparticulates that can encapsulate high drug payloads and provide tunable release profiles, with demonstrated applications spanning transdermal patches, wound-healing matrices, and intraperitoneal cancer therapy (36). Together, these complementary technologies signal a manufacturing paradigm shift that is likely to underpin the next wave of clinically viable, patient-specific drug delivery products (33).

E. Emerging Delivery Routes/Applications:

A growing repertoire of delivery routes and therapeutic modalities is expanding the clinical reach of CDD. Stimuli-responsive platforms continue to evolve, incorporating increasingly sophisticated sensing mechanisms that link drug discharge to precise physiological and pathological cues, enabling fine temporal and spatial control over dosing (37,38). Parallel advances in nanotechnology have yielded biodegradable nanocarriers with improved targeting fidelity and reduced off-target toxicity, further broadening the scope of treatable indications (7,37). The emergence of remotely actuated pulsatile systems—encompassing electro-responsive, magnetically controlled, and acoustically triggered platforms—now permits fully on-demand drug administration, a feature of particular value in conditions requiring rapid therapeutic adjustment (37). These innovations collectively pave the way for highly individualized, combination-based treatment architectures that address the fundamental limitations of fixed-dose conventional therapy (39).

IV. CHALLENGES AND LIMITATIONS IN CONTROLLED DRUG DELIVERY

Despite impressive technological momentum, the clinical translation of CDD systems remains beset by interconnected challenges spanning biology, safety, manufacturing, and regulation.

A. Biological Barriers:

The in vivo performance of any CDD system is fundamentally constrained by the body's endogenous defensive architecture. Physiological gatekeepers—including mucus layers, the blood-brain barrier (BBB), and the glycocalyx that coats cell surfaces—act in concert to limit carrier access to target tissues and impede cellular internalization (40,41). Immunological defenses compound

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this problem: recognition of nanoparticulate carriers by circulating mononuclear phagocytes leads to rapid systemic clearance, dramatically shortening the window of therapeutic opportunity (40). Target site heterogeneity—arising from anatomical variability, disease-stage-dependent perfusion, and inter-patient differences in receptor expression—further compounds the challenge of reliable drug delivery (42,43). A mechanistic understanding of these biological barriers is indispensable for optimizing carrier design, particularly when targeting immunologically privileged or highly heterogeneous environments such as solid tumors and the CNS (42,44).

B. Safety and Toxicity Concerns:

The complexity of CDD systems introduces a distinct safety profile that demands careful evaluation. Key concerns include the potential cytotoxicity of carrier materials, incompatibility of degradation byproducts with host tissues, and the risk of inflammatory reactions following implantation or repeated parenteral administration (5). For implantable devices, the additional procedural risks of surgical insertion and extraction—including infection and tissue trauma—must be factored into the risk-benefit calculus. The intricate release mechanisms of many CDD platforms can also generate unpredictable fluctuations in drug exposure, raising the spectre of underdosing or toxicity (45,46). From a health economics standpoint, the elevated development and manufacturing costs of advanced CDD systems relative to conventional formulations may restrict patient access and limit adoption in resource-constrained settings. A rigorous and systematic assessment of these safety dimensions is a prerequisite for responsible clinical deployment of CDD technologies (5,47).

C. Clinical Translation Gap:

The pathway from laboratory proof-of-concept to clinical utility is strewn with substantive obstacles for CDD systems. A recurring challenge is the poor predictive value of simplified experimental models: the enhanced permeability and retention (EPR) effect, for example, which underpins passive nanoparticle targeting in rodent models, is far less reliable in human tumors (48). The field also suffers from a lack of standardized in vitro–in vivo correlation methodologies and insufficient cross-disciplinary collaboration between bench scientists and clinical practitioners, resulting in a disproportionate emphasis on cell-based studies that lack in vivo validity (49). For CNS indications, the inherent heterogeneity of human neurological disease makes extrapolation from animal models particularly unreliable, and the pharmacokinetic complexities of achieving meaningful CNS drug exposure must be resolved prior to clinical trial (50,51). Scalable manufacturing, cost-competitive production, and the navigation of multi-jurisdictional regulatory frameworks represent additional hurdles that must be systematically addressed before these technologies can achieve broad adoption (52).

V. FUTURE DIRECTIONS AND OUTLOOK

Future research will increasingly leverage data-driven computational tools—particularly AI and ML—to accelerate formulation discovery and predict clinical performance with greater fidelity.

A. Personalized and Precision Medicine:

CDD is increasingly recognized as a key enabling technology for precision medicine, providing the delivery infrastructure needed to actualize individualized treatment protocols. Technologies including polymeric nanoparticles, implantable matrices, and three-dimensional-printed drug products allow for precise, sustained therapeutic delivery with minimized systemic exposure (38,53). Advances in nanomedicine provide the resolution needed to direct drugs to specific cell populations within complex tissues, limiting off-target pharmacological activity (54). The integration of pharmacogenomic data into formulation design—matching drug release parameters to patient-specific genetic polymorphisms that govern drug metabolism and receptor sensitivity—moves CDD firmly into the precision medicine paradigm (7,53). Although formulation complexity and evolving regulatory expectations remain challenges, the combined momentum of smart materials development and biodegradable polymer science positions CDD as a central pillar of patient-centered therapeutic innovation (39,54).

B. Artificial Intelligence and Machine Learning in CDD:

AI and ML are reshaping the CDD development pipeline by providing powerful tools for navigating the high-dimensional parameter space of formulation design. AI-driven analysis of multi-omics datasets accelerates the identification of actionable disease targets and enables rational selection of drug candidates with favorable interaction profiles for specific patient populations (55). Gradient-boosting algorithms such as XGBoost and LightGBM have demonstrated strong performance in predicting optimal carrier composition and release parameters from patient characteristic inputs (56). Across the development timeline, AI-assisted optimization has been reported to compress formulation development cycles by 40–60% and enhance bioavailability prediction accuracy by 15–25% (57). Integrated multi-descriptor ML models deepen mechanistic understanding of drug-matrix interactions, ultimately guiding the design of more stable, efficient, and patient-responsive delivery platforms (58). Notwithstanding these advances, the limited availability of high-quality training datasets and lingering regulatory uncertainty regarding AI-assisted development submissions remain significant barriers to widespread adoption (57,58).

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C. Regulatory Framework Evolution:

The regulatory landscape governing CDD systems is in active transition, driven by the rapid pace of technological innovation and the escalating complexity of the product types entering development pipelines. Stimulus-responsive biomaterials and nanoparticulate carriers challenge existing classification schemes and necessitate the development of new paradigms for demonstrating consistent safety and efficacy (5,7). Mechanistically complex release systems—encompassing diffusion, erosion, osmotic pumping, and enzymatic degradation—require sophisticated and individualized evaluation frameworks to ensure therapeutic reliability (38,59). The emergence of intelligent drug delivery systems (IDDS) that simultaneously exhibit characteristics of devices, biologics, and drugs creates regulatory ambiguity that existing frameworks are ill-equipped to resolve without further evolution (60). Patient-level variability in physiology and genetics introduces additional unpredictability that regulatory assessments must account for. As personalized and remotely controllable delivery technologies proliferate, agencies such as the US FDA will need to develop adaptive, risk-proportionate frameworks that balance therapeutic innovation with robust safeguards for patient welfare (59,60).

VI. CONCLUSION

The controlled drug delivery field has undergone a profound transformation, progressing from simple extended-release tablets to sophisticated, stimuli-programmable nanocarrier systems with the capacity for tissue-selective, on-demand drug deployment. The most consequential developments of recent years include the engineering of nanotechnology-based carriers—liposomes, polymeric nanoparticles, and dendrimers—that offer markedly improved bioavailability and targeting precision in oncological settings, and the emergence of SRDDS that couple drug release to physiological disease signals rather than passive diffusion. Complementary manufacturing innovations using microfluidic and electrospinning platforms have enabled the reproducible production of carriers with tightly controlled physicochemical properties.

These sustained delivery platforms maintain drug plasma levels within the therapeutic window over extended periods, reducing both adverse effects and the dosing frequency that frequently undermines adherence in chronic disease management.

Nonetheless, substantial hurdles must still be navigated. The body's multilayered biological defenses—including immune surveillance, tight-junction barriers, and mucosal clearance mechanisms—continue to impede effective delivery to deep target sites. Safety concerns around material biocompatibility and the predictability of drug release kinetics require ongoing scrutiny to prevent harmful dosing deviations. Bridging the clinical translation gap will demand the standardization of in vitro–in vivo correlations, tighter integration between materials scientists and clinical investigators, and robust manufacturing and regulatory strategies capable of supporting first-in-human trials.

The long-range outlook for CDD is highly promising. The convergence of advanced delivery technologies with AI- and ML-driven formulation science will accelerate both development timelines and the capacity to tailor therapies to individual patient profiles. Continued scientific rigor and a proactive, adaptive regulatory posture are essential if these transformative technologies are to move efficiently and safely from the bench to routine clinical practice—ultimately delivering more targeted, efficacious, and safer treatments for patients worldwide.

REFERENCES

[1]. Siepmann J, Siepmann F. Modeling of diffusion controlled drug delivery. J Controlled Release. 2012 July 20;161(2):351–62.
[2]. Loke YH, Jayakrishnan A, Razif MRFM, Yee KM, Kee PE, Goh BH, et al. A Comprehensive Review of Challenges in Oral Drug Delivery Systems and Recent Advancements in Innovative Design Strategies. http://www.eurekaselect.com [Internet]. [cited 2025 Sept 1]; Available from: https://www.eurekaselect.com/article/143781
[3]. Virmani T, Kumar G, Sharma A, Pathak K. An overview of ocular drug delivery systems—conventional and novel drug delivery systems. In: Nanotechnology in Ophthalmology [Internet]. Elsevier; 2023 [cited 2025 Sept 1]. p. 23–48. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780443152641000075
[4]. Novel Drug Delivery Systems: An Important Direction for Drug Innovation Research and Development [Internet]. [cited 2025 Sept 1]. Available from: https://www.mdpi.com/1999-4923/16/5/674
[5]. Hamzy IA, Alqhoson AI, Aljarbou AM, Alhajri MA. An in-depth overview of controlled drug delivery systems: Present developments and prospective advancements. Int J Health Sci. 2022 Jan 15;6(S10):1755–70.
[6]. http://www.eurekaselect.com [Internet]. [cited 2025 Sept 1]. Controlled Drug Delivery Systems: Concepts and Rationale. Available from: http://www.eurekaselect.com/chapter/23899
[7]. Chaudhary NK, R. Rajbhar MrR, Dr. RashidIqbal DrR. "Controlled Drug Delivery System." Int J Pharm Res Appl. 2025 Apr;10(4):277–88.
[8]. Swarnalatha KM, Iswariya VT, Akash B, Bhandari S, Shirisha R, Ramarao T. A Comprehensive Review of Controlled Drug Release Delivery Systems: Current Status and Future Directions. Int J Pharm Phytopharm Res. 2024;14(2–2024):24–30.
[9]. Kanaujia I. ADVANCED DRUG DELIVERY SYSTEM. In: Philip DrS, Vatsa DrE, Prajapati R, R Karthi, B GBhavani, Swain MP, et al., editors. Futuristic Trends in Pharmacy & Nursing Volume 3 Book 10 [Internet]. First. Iterative International Publisher, Selfypage Developers Pvt Ltd; 2024 [cited 2025 Oct 15]. p. 163–82. Available from: https://www.iipseries.org/viewpaper.php?pid=3056&pt=advanced-drug-delivery-system

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr1847

[10]. Kumari S, R Rajbhar MrR. Controlled drug delivery systems. Int J Pharm Res Appl. 2025 Apr;10(4):309–16.
[11]. Mehrotra S, Pathak K. Chapter 1 - Controlled release drug delivery systems: principles and design. In: Nayak AK, Sen KK, editors. Novel Formulations and Future Trends [Internet]. Academic Press; 2024 [cited 2025 Oct 15]. p. 3–30. Available from: https://www.sciencedirect.com/science/article/pii/B978032391816900014X
[12]. Guo X, Luo Z, Cui H, Wang J, Jiang Q. A novel and reproducible release mechanism for a drug-delivery system in the gastrointestinal tract. Biomed Microdevices. 2019 Feb 27;21(1):25.
[13]. Sinha VR, Sharma S, Silki, Kaur M, Sarwal A. 6 - Current Polyesteric Systems for Advanced Drug Delivery. In: Holban AM, Grumezescu AM, editors. Nanoarchitectonics for Smart Delivery and Drug Targeting [Internet]. William Andrew Publishing; 2016 [cited 2025 Oct 15]. p. 143–68. Available from: https://www.sciencedirect.com/science/article/pii/B9780323473477000069
[14]. Saranya S, Radha KV. Review of Nanobiopolymers for Controlled Drug Delivery. Polym-Plast Technol Eng. 2014 Oct 30;53(15):1636–46.
[15]. Narasimhan B, Kipper MJ. SURFACE-ERODIBLE BIOMATERIALS FOR DRUG DELIVERY. In: Advances in Chemical Engineering [Internet]. Academic Press; 2004 [cited 2025 Oct 15]. p. 169–218. (Advances in Chemical Engineering: Molecular and Cellular Foundations of Biomaterials; vol. 29). Available from: https://www.sciencedirect.com/science/article/pii/S0065237703290062
[16]. Bao H, Wang N, Guo J, Han X. Applications of Biodegradable Polymeric Nanomaterials as Drug Delivery Systems. http://www.eurekaselect.com [Internet]. [cited 2025 Oct 15]; Available from: https://www.eurekaselect.com/article/149750
[17]. Faculty of Pharmacy Kampala International University Uganda, Nankya W. Nanotechnology in Cancer Treatment: Targeted Drug Delivery. Res Output J Public Health Med. 2024 Nov 23;4(2):38–42.
[18]. Pranita Sanjay Dudhe, Rutuja Thakare. Targeted Drug Delivery in Cancer Therapy. Int J Adv Res Sci Commun Technol. 2024 Dec 4;109–24.
[19]. Sengar A. The Role of Nanotechnology in Revolutionizing Cancer Treatment [Internet]. Preprints; 2025 [cited 2025 Oct 15]. Available from: https://www.preprints.org/manuscript/202503.0713/v1
[20]. Mittal M, Juneja S, Pandey N, Mittal R. Nanoparticle-Based Drug Delivery Systems: Current Advances and Future Directions. Curr Drug Targets. 26:1–23.
[21]. Nandhini Chitikela, Chaitanya B. Current Advances in Nanotechnology-Based Drug Delivery Systems: Review Article. J Pharma Insights Res. 2025 Feb 5;3(1):327–34.
[22]. Kallepalli B, Garg U, Jain N, Nagpal R, Malhotra S, Tiwari T, et al. Intelligent Drug Delivery: Pioneering Stimuli-Responsive Systems to Revolutionize Disease Management- An In-depth Exploration. Curr Drug Deliv. 22(2):195–214.
[23]. Lopes JR, Santos G, Barata P, Oliveira R, Lopes CM. Physical and Chemical Stimuli-Responsive Drug Delivery Systems: Targeted Delivery and Main Routes of Administration. http://www.eurekaselect.com [Internet]. [cited 2025 Oct 15]; Available from: https://www.eurekaselect.com/article/56368
[24]. Subramanian J, Padhy R, Arun J, Murthannagari VR, Gnk G. STIMULI-RESPONSIVE DRUG DELIVERY SYSTEMS: EXTENSIVE OVERVIEW. Int J Appl Pharm. 2025 Sept 7;94–106.
[25]. Patel K, Patel N, Gupta MA, Patel CN. An Overview on Stimuli Sensitive Drug Delivery System. Int J Innov Sci Res Technol IJISRT. 2024 Mar 13;1788–94.
[26]. Wang ZY, Song J, Zhang DS. Nanosized As2 O3 /Fe2 O3 complexes combined with magnetic fluid hyperthermia selectively target liver cancer cells. World J Gastroenterol. 2009;15(24):2995.
[27]. Mateen MAM, Hatwar PR, Solanki TV, Bakal RL, Karule VG, Mateen MAM, et al. Targeted drug delivery in cancer therapy: A promising approach for effective treatment. GSC Biol Pharm Sci. 2025;32(3):132–40.
[28]. Macadangdang RR, Agrawal R, Bhushan B, Garg A, Singh K, Kumar S, et al. Nanotechnology Integrated Innovative Drug Delivery and Therapy for Cancer. Curr Pharm Biotechnol. 26(8):1189–206.
[29]. Dasram MH, Walker RB, Khamanga SM. Recent Advances in Endocannabinoid System Targeting for Improved Specificity: Strategic Approaches to Targeted Drug Delivery. Int J Mol Sci. 2022 Jan;23(21):13223.
[30]. Yu H, Yang Z, Li F, Xu L, Sun Y. Cell-mediated targeting drugs delivery systems. Drug Deliv. 2020 Jan 1;27(1):1425–37.
[31]. Haq M MU. Revolutionizing Drug Delivery: Targeted Approaches and Innovations for Effective Treatment. Pharm Drug Regul Aff J. 2023 June 29;6(1):1–8.
[32]. Velmurugan K, Kulkarni MB, Gupta I, Das R, Goel S, Nirmal J. Role of Microfluidics in Drug Delivery. In: Mohanan PV, editor. Microfluidics and Multi Organs on Chip [Internet]. Singapore: Springer Nature; 2022 [cited 2025 Oct 15]. p. 107–33. Available from: https://doi.org/10.1007/978-981-19-1379-2_5
[33]. Mohammadi M, Ahmed Qadir S, Mahmood Faraj A, Hamid Shareef O, Mahmoodi H, Mahmoudi F, et al. Navigating the future: Microfluidics charting new routes in drug delivery. Int J Pharm. 2024 Apr;124142.
[34]. Aceves-Serrano LG, Ordaz-Martinez KA, Vazquez-Piñon M, Hwang H. Microfluidics for drug delivery systems. In: Nanoarchitectonics in Biomedicine [Internet]. Elsevier; 2019 [cited 2025 Oct 15]. p. 55–83. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780128162002000025
[35]. Chakraborty R, Parvez S. Microfluidics in Drug Delivery. In: Mohanan PV, editor. Microfluidics and Multi Organs on Chip [Internet]. Singapore: Springer Nature; 2022 [cited 2025 Oct 15]. p. 135–62. Available from: https://doi.org/10.1007/978-981-19-1379-2_6
[36]. Alkhatib H, Rahal OA, Hossain MS, Mawazi SM. Recent Advances in Electrospraying and Electrospinning Technologies. In: Electrospraying and Electrospinning in Drug Delivery. CRC Press; 2025.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr1847

[37]. Kaliki IS, Kabissa JP, Singh PK, Sharma S. Advances in Drug Delivery Systems: Review Article. J Pharma Insights Res. 2024 June 6;2(3):088–95.
[38]. Pillai A, Bhande D, Pardhi V. Controlled Drug Delivery System. In: Santra TS, Shinde AUS, editors. Advanced Drug Delivery: Methods and Applications [Internet]. Singapore: Springer Nature; 2023 [cited 2025 Oct 15]. p. 267–89. Available from: https://doi.org/10.1007/978-981-99-6564-9_11
[39]. Jangid A kumar, Dev R, Sharma S, Bhatnagar P. REVOLUTIONIZING THERAPEUTICS: ADVANCES, CHALLE- NGES, AND FUTURE HORIZONS IN CONTROLLED RELEASE DRUG DELIVERY SYSTEMS. Curr Res Pharm Sci. 2025 Aug 14;20–39.
[40]. Barzegar-fallah A, Houlton J, Barwick D, Shavandi A, Ali MA, Clarkson AN, et al. Chapter 19 - From barriers to bridges; glycans in nonparenteral nanomedicines. In: Kesharwani P, Taurin S, Greish K, editors. Theory and Applications of Nonparenteral Nanomedicines [Internet]. Academic Press; 2021 [cited 2025 Oct 16]. p. 467–87. Available from: https://www.sciencedirect.com/science/article/pii/B9780128204665000193
[41]. Vanshita, Garg A, Dewangan HK. Recent Advances in Drug Design and Delivery Across Biological Barriers Using Computational Models. http://www.eurekaselect.com [Internet]. [cited 2025 Oct 16]; Available from: https://www.eurekaselect.com/article/120675
[42]. Narayanaswamy R, Attia SA, Torchilin VP. Parameters and Strategies to Overcome Barriers to Systemic Delivery. In: Lai WF, editor. Systemic Delivery Technologies in Anti-Aging Medicine: Methods and Applications [Internet]. Cham: Springer International Publishing; 2020 [cited 2025 Oct 16]. p. 447–75. Available from: https://doi.org/10.1007/978-3-030-54490-4_19
[43]. Rubinstein A, Robinson JR. Controlled Drug Delivery. In: Debus E, Grossmann CJ, Hubbuch AP, Lanners HN, Linke R, Perkins ME, et al., editors. Control of Immune Response by Endocrine Factors Malaria Vaccine Controlled Drug Delivery Enzyme-Immunoassay. Berlin, Heidelberg: Springer; 1987. p. 71–107.
[44]. Voronin DV, Abalymov AA, Svenskaya YI, Lomova MV. Key Points in Remote-Controlled Drug Delivery: From the Carrier Design to Clinical Trials. Int J Mol Sci. 2021 Jan;22(17):9149.
[45]. Adepu S, Ramakrishna S. Controlled Drug Delivery Systems: Current Status and Future Directions. Molecules. 2021 Jan;26(19):5905.
[46]. Gunisetty H, Balagani PK. Transdermal Drug Delivery System: An Update of Upcoming Evolution. J Compr Pharm. 2016;03(01):23–33.
[47]. Shukla SS, Pandey RK, Kalyani G, Shukla SS, Pandey RK, Kalyani G. https://services.igi-global.com/resolvedoi/resolve.aspx?doi=10.4018/978-1-7998-8908-3.ch008. IGI Global Scientific Publishing; 1 AD [cited 2025 Oct 16]. Controlled Drug Delivery Systems: Contemporary Significance and Advances – Overview and Advances for Controlled Drug Delivery Systems. Available from: https://www.igi-global.com/gateway/chapter/www.igi-global.com/gateway/chapter/300406
[48]. Nayak R, Meerovich I, Dash AK. Translational Multi-Disciplinary Approach for the Drug and Gene Delivery Systems for Cancer Treatment. AAPS PharmSciTech. 2019 Apr 9;20(4):160.
[49]. Pircalabioru GG, Chifiriuc MC. Nanoparticulate Drug-Delivery Systems for Fighting Microbial Biofilms: From Bench to Bedside. Future Microbiol. 2020 May;15(8):679–98.
[50]. Steeves JD. Chapter 11 - Bench to bedside: challenges of clinical translation. In: Dancause N, Nadeau S, Rossignol S, editors. Progress in Brain Research [Internet]. Elsevier; 2015 [cited 2025 Oct 16]. p. 227–39. (Sensorimotor Rehabilitation; vol. 218). Available from: https://www.sciencedirect.com/science/article/pii/S0079612314000417
[51]. Ronaldson PT, Williams EI, Betterton RD, Stanton JA, Nilles KL, Davis TP. CNS Drug Delivery in Stroke: Improving Therapeutic Translation From the Bench to the Bedside. Stroke. 2024 Jan;55(1):190–202.
[52]. Hua S, de Matos MBC, Metselaar JM, Storm G. Current Trends and Challenges in the Clinical Translation of Nanoparticulate Nanomedicines: Pathways for Translational Development and Commercialization. Front Pharmacol [Internet]. 2018 July 17 [cited 2025 Oct 16];9. Available from: https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2018.00790/full
[53]. Thore PP, Bhatjire GS, Shirsath VV, Jadhav AG. Innovations in pharmaceutical formulation and delivery system [Internet]. Deep Science Publishing; 2025 [cited 2025 Oct 16]. Available from: https://www.deepscienceresearch.com/dsr/catalog/book/209/chapter/835
[54]. Shaikh S, Satpute, R, Satpute A, Omkar S, Pawar MrV. "A Perceptive Review on Advancement in Drug Delivery System". Int J Pharm Res Appl. 2024 May;09(05):495–504.
[55]. Vora LK, Gholap AD, Jetha K, Thakur RRS, Solanki HK, Chavda VP. Artificial Intelligence in Pharmaceutical Technology and Drug Delivery Design. Pharmaceutics. 2023 July;15(7):1916.
[56]. Wang Y, Shao W, Lin J, Zheng S. Intelligent Drug Delivery Systems: A Machine Learning Approach to Personalized Medicine [Internet]. Engineering; 2025 [cited 2025 Oct 16]. Available from: https://www.preprints.org/manuscript/202504.2570/v1
[57]. Oladosu MA, Abah MA, Agbo LI, Akinwande PS, Babalola MT, Imitini IOE Delta State, Nigeria, et al. Role of Artificial Intelligence in Oral Drug Delivery Optimization: A Systematic Review of Current Applications and Future Perspectives (Preprint) [Internet]. JMIR AI; 2025 [cited 2025 Oct 16]. Available from: http://preprints.jmir.org/preprint/79287
[58]. Ravindran R, Muthusamy S, Mohan AA. Machine Learning in Formulation Development and Optimization of Controlled Drug Delivery Systems. In: Vijaykumar H, Urbana Ivy BP, Kumar RR, G N, editors.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26apr1847

Multidisciplinary Engineering Applications of Artificial Intelligence in Design Control and Infrastructure Systems [Internet]. 2025th ed. RADemics Research Institute; 2025 [cited 2025 Oct 16]. p. 339–62. Available from: https://www.rademics.com/chapter.php?id=67&cid=12

[59]. Prajapati VD, Shrivastav P, Suthar K. Controlled Drug Delivery Systems: Concepts and Rationale. In: Mundada AS, Chaudhari A, editors. Novel Drug Delivery Systems (Part 1) [Internet]. BENTHAM SCIENCE PUBLISHERS; 2024 [cited 2025 Oct 16]. p. 1–38. Available from: https://www.eurekaselect.com/node/236753

[60]. Sapsford KE, Lauritsen K, Tyner KM. Current Perspectives on the US FDA Regulatory Framework for Intelligent drug-delivery Systems. Ther Deliv. 2012 Dec 1;3(12):1383–94