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LONG-ACTING THERAPIES TRANSFORMING APPROACHES TO CHRONIC DISEASE MANAGEMENT: A COMPREHENSIVE REVIEW

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Keywords	***Abstract***
Long-Acting Therapeutics; Long-Acting Injectables; Drug Delivery Systems; Chronic Disease Management; Medication Adherence; Sustained-Release Formulations; Depot Injections; Pharmacokinetics; Precision Medicine; Controlled Drug Delivery.	Chronic diseases remain a leading cause of global morbidity and mortality, with medication non-adherence representing a major barrier to achieving optimal therapeutic outcomes. Long-acting therapeutic systems have emerged as a transformative strategy to overcome the limitations of conventional daily dosing by providing sustained drug release over extended periods. This review comprehensively examines the evolution, pharmacological principles, formulation technologies, clinical applications, and future prospects of long-acting drug delivery systems. It highlights the mechanisms underlying prolonged drug release through depot injections, biodegradable implants, polymeric microspheres, nanosuspensions, and stimuli-responsive biomaterials, emphasizing their ability to maintain stable therapeutic drug concentrations, reduce dosing frequency, and improve patient adherence. The review further explores the expanding clinical utility of long-acting therapies across infectious diseases, cardiovascular disorders, diabetes, neuropsychiatric illnesses, and immunological conditions, where sustained drug exposure has demonstrated improvements in treatment

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	persistence and disease control. Emerging innovations, including artificial intelligence-assisted formulation design, smart biomaterials, 3D-printed implants, and programmable gene- and cell-based delivery platforms, are discussed as promising technologies that may redefine precision medicine. Despite these advances, important challenges remain, including manufacturing complexity, regulatory considerations, healthcare infrastructure requirements, reimbursement models, and equitable global access. By integrating current evidence from pharmaceutical sciences, pharmacokinetics, and clinical research, this review highlights the transformative potential of long-acting therapeutic platforms to improve adherence, optimize clinical outcomes, and reshape chronic disease management while identifying key priorities for future research and clinical implementation.

Introduction

The global escalation of chronic disease prevalence has underscored significant limitations in daily oral regimens, where patient non-adherence frequently undermines therapeutic efficacy. Estimates indicate that between 30% and 50% of adults with chronic conditions fail to take their medications as prescribed, a pattern directly correlated with roughly 125,000 preventable deaths and approximately 10% of all hospitalisations in the United States each year (Pons-Faudoa et al., 2019, p. 48). The economic burden paralleling these clinical consequences is similarly staggering, with non-adherence alone accounting for an estimated $310 billion in avoidable U.S. healthcare expenditures annually through disease progression, complications, and unnecessary resource utilisation . Contributing factors are multifactorial and include regimen complexity, cumulative pill burden, forgetfulness, socioeconomic constraints, adverse effects tied to peak-trough plasma fluctuations, and intentional disengagement stemming from inadequate disease literacy or insufficient patient–provider communication (Burnier, 2023; Patel et al., 2025). These persistent challenges have catalysed a paradigm shift toward long-acting therapeutic platforms — spanning depot injectables, biodegradable implants, and extended-release formulations — designed to sustain therapeutic drug concentrations over weeks to months, thereby reducing dosing frequency and removing the day-to-day reliance on patient-driven administration (Chaudhary et al., 2018; Kumar et al., 2020). By decoupling pharmacologic exposure from daily behavioural demands, such approaches aim to stabilise pharmacokinetic profiles, attenuate adherence-related outcome gaps, and ultimately redefine chronic disease management across infectious, metabolic, cardiovascular, and neuropsychiatric indications (Rathore & Singh, 2025). This evolution in therapeutic delivery leverages diverse technologies, including nanosuspensions, polymeric microspheres, and in situ-forming implants, to address the systemic pharmacokinetic challenges associated with rapid drug clearance (Larrañeta & Domínguez-Robles, 2025; Nkanga et al., 2020, p. 20).

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This review delineates the technological trajectory of these platforms, tracing their evolution from legacy, oil-based solutions to sophisticated, bio-responsive carriers engineered to optimise release kinetics and prolong therapeutic drug exposure.

Review Scope and Objectives

Beyond tracing this trajectory, this article systematically evaluates the core pharmacological underpinnings and therapeutic efficacy of these systems, while simultaneously addressing the multifaceted clinical implementation barriers—spanning regulatory complexities, manufacturing hurdles, and patient-provider dynamics—that dictate their real-world utility (Mahajan et al., 2025; Sawale et al., 2026). Through this rigorous synthesis, the review establishes a comprehensive framework to assess the transformative potential of long-acting delivery in optimizing management protocols across diverse chronic infectious, metabolic, cardiovascular, and neuropsychiatric indications, ultimately aiming to translate advanced formulation science into sustainable clinical improvements (Rathore & Singh, 2025; THEYANESHWARAN et al., 2025).

The analysis methodology prioritizes a cross-disciplinary synthesis, examining clinical data from randomized controlled trials alongside pharmacokinetic modeling to quantify the impact of sustained-release kinetics on relapse rates and therapeutic adherence (Yuan et al., 2023, p. 403).Furthermore, this review evaluates the development of predictive in vitro dissolution methods as a critical surrogate for estimating in vivo performance, establishing a standardized quality assessment framework essential for the broad clinical adoption of these depot parenteral systems (Alidori et al., 2024; THEYANESHWARAN et al., 2025). By integrating these multifaceted analytical dimensions, the review further underscores the role of robust in vitro-in vivo correlation models in facilitating regulatory approval and accelerating the translation of innovative delivery platforms into standardized therapeutic care (Markowicz-Piasecka et al., 2023). This synthesis additionally addresses the inherent risks associated with manufacturing scale-up and formulation stability, such as the potential for unforeseen adverse events linked to dose dumping or unexpected pharmacokinetic variability (Wen et al., 2015, p. 1334).

Pharmacology of Long-Acting Agents

The therapeutic efficacy of these systems relies on the precise modulation of absorption kinetics, achieved through advanced mechanisms such as depot injections, biodegradable polymer implants, and nanoparticle-based delivery (Rahnfeld & Luciani, 2020). These formulation matrices utilize biodegradable polymers and microsphere technologies to create a controlled-release environment that extends the drug's elimination half-life, effectively smoothing out plasma concentration fluctuations (Shi et al., 2021; Siemons et al., 2023, p. 99). By facilitating sustained drug release through drug diffusion, osmosis, or carrier dissolution, these systems effectively decouple a drug's intrinsic half-life from its apparent clinical half-life (Gandhi, 2025; Sillman et al., 2018, p. 445). This

refined approach leverages the structural properties of materials such as polylactic-co-glycolic acid and drug nanocrystals to maintain consistent therapeutic levels, thereby mitigating the risk of sub-therapeutic troughs and drug-related toxicities (Gandhi, 2025; Nwankwo et al., 2024, p. 841).

Specifically, these engineered matrices allow for the programmable degradation of carrier materials or the controlled dissolution of poorly soluble drug salts, enabling dosing intervals that extend from several weeks to multiple months (Correll et al., 2021, p. 39; Jain et al., 2019, p. 323). This modulation of absorption kinetics significantly alters the drug's apparent elimination half-life, ensuring that systemic levels remain within the therapeutic window despite rapid intrinsic metabolic clearance (Bannigan et al., 2023, p. 35; Holm et al., 2023, p. 53). Such precise control over release rates frequently necessitates the use of complex parenteral formulations, where both the physicochemical properties of the excipients and the nuances of the manufacturing process dictate the final pharmacokinetic behavior (Selmin et al., 2019, p. 323).

Mechanisms of Sustained Release

These release mechanisms are fundamentally governed by the interplay of slow dissolution, controlled diffusion, and enzymatic degradation, which dictate the transition of active pharmaceutical ingredients from the injection site into systemic circulation (THEYANESHWARAN et al., 2025). By tailoring the physicochemical attributes of the delivery system—such as particle size, polymer composition, and matrix porosity—formulators can exert precise control over the drug release profile, effectively mitigating the rapid clearance typical of conventional parenteral administration (Larrañeta & Domínguez-Robles, 2025; Shi et al., 2021). In biodegradable polymeric systems, for instance, matrix erosion—often through hydrolysis or enzymatic degradation—progresses in concert with drug diffusion to ensure sustained, prolonged therapeutic concentrations (Bannigan et al., 2023, p. 35; Gandhi, 2025). Conversely, for crystalline suspensions, the rate-limiting step frequently involves the slow dissolution of the drug particles, an attribute critically dependent on particle surface area and the local environment's solubility dynamics (Holm et al., 2023, p. 53; Jain et al., 2019, p. 323). Such meticulous modulation of these fundamental processes is essential to achieve a stable pharmacokinetic profile, ensuring that drug levels remain within the therapeutic window while minimizing the risk of sub-therapeutic troughs or toxic peak exposures (Gandhi, 2025; Wen et al., 2015, p. 1334).

Furthermore, the integration of microparticle and implantable technologies enables the design of systems capable of maintaining effective concentrations for extended durations, potentially reaching several months or longer. These advanced platforms leverage sophisticated material architectures to precisely tune drug release kinetics, thereby streamlining management protocols for chronic conditions and significantly reducing the clinical burden associated with frequent dosing requirements (Larrañeta & Domínguez-Robles, 2025; Rathore & Singh, 2025; THEYANESHWARAN et al., 2025). However, achieving such prolonged efficacy necessitates

careful management of the initial burst release, which can occur as drug molecules near the matrix surface diffuse rapidly into the surrounding tissue (Shen & Burgess, 2012, p. 988; Yun et al., 2015, p. 7).

Novel Formulation Technologies

Emerging frontiers in parenteral delivery are transcending traditional passive-release platforms by leveraging stimuli-responsive materials—such as biomaterials engineered to undergo precise phase transitions triggered by physiological signals like localized pH shifts, temperature gradients, or specific enzymatic activities—to achieve feedback-regulated, 'on-demand' drug release (Alvarez-Lorenzo & Concheiro, 2014; THEYANESHWARAN et al., 2025). Complementing these smart biomaterials, the adoption of advanced fabrication techniques like 3D printing allows for the construction of personalized, complex-geometry implants capable of achieving highly orchestrated, multi-phasic kinetics that are largely unattainable via conventional manufacturing (Larrañeta & Domínguez-Robles, 2025; Zhu et al., 2025). Furthermore, the integration of artificial intelligence and machine learning into formulation science is revolutionizing this design space, enabling the predictive optimization of polymer-drug interactions and critical process parameters to effectively mitigate initial burst effects while maximizing therapeutic consistency over ultra-long durations (Bannigan et al., 2023, p. 35; Ros et al., 2026).

In addition, these computational strategies facilitate the rapid evaluation of microsphere architectures and in situ forming gels, which serve as highly adaptable scaffolds for localized or systemic delivery (Bannigan et al., 2023, p. 35). By employing high-throughput screening and predictive modeling, researchers can iteratively refine formulation parameters—such as polymer molecular weight, drug-to-polymer ratios, and solvent selection—before experimental synthesis, thereby streamlining the path from design to clinical translation (Ros et al., 2026; Zhu et al., 2025). Such data-driven methodologies not only reduce the reliance on time-intensive, trial-and-error approaches but also provide deeper insights into the complex, nonlinear relationships between formulation composition and release behavior, paving the way for more robust and personalized parenteral therapies. Furthermore, the transition toward prodrug approaches and modular biomaterial-based platforms offers additional versatility in controlling the temporal delivery of therapeutic payloads (Benhabbour et al., 2019, p. 4324).

Pharmacokinetic and Dynamic Profiles

In this kinetic paradigm—often termed "flip-flop" pharmacokinetics—the absorption rate from the depot becomes the rate-limiting step governing the terminal slope of the plasma concentration-time curve, rendering time to steady state a function of release kinetics and steady-state concentration a function of elimination, while patient-specific covariates such as injection-site vascularity, subcutaneous adiposity, body weight, CYP2D6 metabolizer status, and the foreign body reaction to

crystalline depots collectively modulate apparent absorption rates and contribute to the substantial interindividual variability observed clinically (Correll et al., 2021, p. 42; Siemons et al., 2023, p. 103; Yáñez et al., 2011, p. 664).

To mitigate these fluctuations, current research focuses on defining precise dosing intervals that align with the specific half-lives and release durations of these advanced delivery matrices (Bannigan et al., 2022, p. 2). Optimal therapeutic outcomes are achieved by characterizing the relationship between steady-state drug levels and the duration of efficacy, ensuring that the dosing interval effectively avoids sub-therapeutic troughs (Bannigan et al., 2022, p. 2). Integrating predictive simulations of biologic bioavailability alongside preclinical modeling of subcutaneous barriers further refines these dosing schedules by accounting for the complex tissue-biomaterial interface (Anselmo et al., 2018, p. 21).

Clinical Applications in Chronic Diseases

This transition necessitates a fundamental recalibration of therapeutic monitoring, as the prolonged presence of drug depots introduces unique clinical complexities that extend beyond simple adherence (Rathore & Singh, 2025; Shi et al., 2021). For instance, in long-acting antiretroviral regimens, while the shift to periodic administration effectively maintains viral suppression (Mantsios et al., 2021, p. 256), the inability to rapidly clear the depot in cases of adverse reactions or potential drug-drug interactions presents a distinct challenge, requiring rigorous management of patient attendance to prevent sub-therapeutic drug levels that could foster viral resistance (Gulick & Flexner, 2018). Similarly, in the management of chronic cardio-metabolic conditions like type 2 diabetes, while injectable glucagon-like peptide-1 receptor agonists provide more sustained glucose control than daily oral therapies (DeYoung et al., 2011, p. 1151; Luginbuhl et al., 2017, p. 4), the inherent pharmacodynamic profile of these depots necessitates precise, clinic-based adjustments to avoid prolonged exposure if patient metabolic sensitivity fluctuates. This same paradigm holds for psychiatric medicine, where the shift to depot antipsychotics or buprenorphine requires new clinical frameworks—moving away from daily pill compliance to structured, longitudinal engagement models that must actively mitigate the risks associated with the prolonged residence of high-potency agents within the patient's system (Llorca et al., 2013, p. 340; Tunagur & Tunagur, 2026).

Specifically, while nanosuspensions have demonstrated superior dosing intervals and viral suppression in infectious disease management (Gulick & Flexner, 2018), the translation of these strategies into psychiatric or metabolic care demands a nuanced balance between durable, patient-centric delivery and the capacity for rapid pharmacological intervention. Unlike antiretroviral therapies where depot stability is paramount for maintaining uninterrupted viral suppression, psychiatric and metabolic applications must account for the dynamic, often unpredictable nature of patient responses, necessitating design architectures that offer potential reversibility or timely termination—through mechanisms such as stimuli-responsive triggered release—to manage adverse

events or sudden shifts in clinical stability without relying solely on the slow, passive degradation of the depot matrix (Alvarez-Lorenzo & Concheiro, 2014; THEYANESHWARAN et al., 2025).

Infectious Disease Applications

In parallel, the extension of long-acting injectables to tuberculosis preventive therapy in latently infected contacts introduces a distinct paradigm in which a single intramuscular dose of nanoparticle-formulated rifabutin or bedaquiline could supplant months of daily oral rifapentine, thereby safeguarding treatment completion and curbing the emergence of drug-resistant tuberculosis in high-burden regions. However, the successful implementation of such long-acting preventive therapies hinges on surmounting distinct pharmacokinetic challenges, particularly the need to achieve sustained therapeutic drug concentrations within mycobacteria-containing granulomas while minimizing the potential for systemic toxicity (Rudolph et al., 2023; Swindells et al., 2018, p. 128). By tailoring the release kinetics and particle characteristics to the specific tissue-pathogen microenvironment, these advanced delivery systems offer a promising pathway to simplify treatment regimens, thereby transforming TB control efforts into more manageable, clinic-centric interventions (Ammerman et al., 2022; Kaushik et al., 2019).

Beyond infectious, psychiatric, and metabolic applications, this therapeutic modality is increasingly expanding into immunopharmacology, where the development of long-acting injectable biologics aims to manage chronic autoimmune conditions. By tailoring the design of these carriers to achieve sustained release of immunomodulatory agents, researchers seek to circumvent the limitations of traditional, non-specific immunosuppressive drugs that require frequent, high-dose administration, thereby enhancing long-term clinical outcomes while reducing the systemic adverse effects often linked to conventional therapeutic delivery (Jawad et al., 2025; Murphy et al., 2024).

Furthermore, the application of long-acting platforms extends to HIV pre-exposure prophylaxis and hepatitis therapy, where the integration of engineered nanosuspensions facilitates superior dosing intervals that significantly improve adherence compared to daily oral regimens (Bassand et al., 2022; Olagunju et al., 2025).

Cardiovascular and Metabolic Uses

Beyond the emerging vaccine-derived and gene-editing platforms for long-acting lipid management, the therapeutic landscape for cardiovascular disease is witnessing a parallel transformation through the advent of RNA interference agents designed for robust blood pressure control. By durably silencing the expression of key drivers such as angiotensinogen—the precursor to all angiotensin peptides—these novel injectable formulations enable multi-month hemodynamic regulation from a single administration (Imbalzano et al., 2025; Sarzani et al., 2023, p. 336). This shift directly addresses the persistent limitations of conventional, daily oral antihypertensives, where non-adherence and therapeutic inertia frequently prevent patients from achieving guideline-recommended

targets (Parvan et al., 2024; Yan et al., 2022, p. 18936). Furthermore, the transition toward provider-administered, long-acting therapeutics like inclisiran for cholesterol management or emerging RNA-targeted agents for hypertension underscores a fundamental move toward clinic-centric care models (Atif et al., 2025; Nishikido, 2023, p. 20). Such approaches not only mitigate the risks of peak-trough variability associated with oral regimens but also leverage structured longitudinal engagement to ensure consistent, durable biometric control in patients with chronic cardio-metabolic conditions (Bajorek et al., 2025; Nishikido, 2023, p. 20).

In the realm of diabetes care, current developments are exploring extended-release injectable peptides that incorporate stimuli-responsive hydrogels to modulate drug flux based on real-time physiological glucose fluctuations (Karabin et al., 2018, p. 625; Magar et al., 2024). These adaptive systems aim to align hormone delivery with the body's intrinsic metabolic demand, potentially reducing the risk of iatrogenic hypoglycemia while optimizing glycemic stability over extended durations (Balogun et al., 2023, p. 1276). These sophisticated formulations build upon established strategies such as protein conjugation and lipidation, which have already proven effective in extending the circulatory half-lives of metabolic peptides like liraglutide and semaglutide (Wang et al., 2022, p. 58). By leveraging microsphere-based delivery systems, these therapeutic analogues have successfully transitioned from twice-daily requirements to once-weekly dosing schedules (Maher et al., 2016, p. 283).

Adherence and Quality of Life

The paradigm shift toward long-acting injectable regimens fundamentally addresses the "dosing burden" that often precipitates therapeutic inertia and poor adherence in chronic disease management (Bajorek et al., 2025; Maher et al., 2016, p. 283). By consolidating treatment into periodic, provider-administered doses, these platforms simplify complex oral regimens that frequently lead to missed doses and sub-optimal therapeutic targets (Atif et al., 2025; Imbalzano et al., 2025). Beyond enhancing pharmacological consistency, this transition can mitigate the psychological fatigue associated with daily medication tasks, potentially improving patient-reported quality of life by reducing the daily visibility of their clinical condition (Balogun et al., 2023, p. 1276; Jawad et al., 2025). Nevertheless, achieving these benefits necessitates a balanced approach that addresses potential patient-level barriers, such as injection-related anxiety or logistical challenges regarding clinic attendance, which remain critical determinants for sustaining long-term therapeutic persistence (Bajorek et al., 2025).

By maintaining a more stable pharmacological profile, these long-acting systems alleviate the cognitive burden of daily medication management and enhance patient-reported quality of life, factors that are indispensable for fostering sustained therapeutic engagement. Clinical evidence increasingly demonstrates that these sustained-release strategies correlate with higher rates of

treatment persistence, particularly in populations where frequent dosing schedules represent a significant barrier to effective disease management (Gilroy et al., 2015, p. 171).

Furthermore, the clinical integration of long-acting antiretroviral therapies and depot-based psychiatric medications has demonstrated that shifting from daily oral administration to intermittent professional oversight significantly reduces the risk of virological rebound and psychiatric relapse, respectively, by effectively mitigating the adherence challenges inherent to complex, daily medication regimens (Endara-Mina et al., 2026; Mahesh et al., 2018; Olivares et al., 2013, p. 38).

Implementation Challenges and Barriers

The widespread adoption of these therapies necessitates substantial investments in clinical infrastructure, particularly regarding the specialized storage, cold-chain management, and injection-site monitoring workflows required for advanced injectable formulations. Beyond logistics, this transition demands a realignment of clinical workflows to accommodate recurring, provider-administered appointments, necessitating significant adjustments in scheduling, nursing support, and documentation standards (Atif et al., 2025). Furthermore, frontline staff require specialized training not only in administration techniques but also in recognizing and managing potential injection-site reactions or delayed systemic responses, which are critical for patient safety (Bajorek et al., 2025). Such operational demands, if not adequately resourced, may constrain the scalability of these regimens and inadvertently widen existing disparities in treatment access between well-resourced centers and resource-limited health systems (Olagunju et al., 2025).

Furthermore, securing the financial viability of these therapies requires evolving current reimbursement frameworks to adequately address the substantial disparity between the high upfront costs of injectable agents and the cost-effective nature of generic oral alternatives (Atif et al., 2025). Policymakers must evaluate incentive structures for pharmacy-based administration to optimize patient access and relieve the clinical burden on specialized care centers (Edwards et al., 2022, p. 14). Moreover, addressing global health inequities remains a paramount challenge, as the high cost of production and specialized cold-chain infrastructure requirements may preclude the adoption of these life-saving technologies in low-resource settings where the burden of chronic disease is most acute (Rajoli et al., 2014, p. 640).

Healthcare System Requirements

To successfully integrate these modalities, health systems must implement automated longitudinal pharmacovigilance registries and interoperable electronic health record monitoring tools to proactively detect and manage delayed systemic responses, which are particularly critical since these therapeutic agents cannot be readily discontinued once administered. Beyond technical infrastructure, this integration facilitates a collaborative care environment where longitudinal data can inform shared decision-making processes, allowing clinicians to tailor treatment plans to

individual patient needs and preferences. Such data-driven approaches not only enhance the reliability of patient-reported outcome monitoring but also enable providers to preemptively address barriers to persistence, such as concerns regarding localized injection discomfort or the burden of recurring clinical interactions. By synthesizing real-time physiological data with patient-centered engagement, health systems can optimize the therapeutic benefits of long-acting formulations, ultimately fostering a more resilient model of care that prioritizes both safety and sustained patient participation.

However, the successful implementation of such models hinges on addressing systemic gaps in care, as existing infrastructure often struggles to meet current guidelines, let alone the added complexities of specialized, longitudinal monitoring (Tobias et al., 2023, p. 2449).

Cost and Access Barriers

The economic viability of these agents is complicated by the potential for significant pharmaceutical budget inflation, which models suggest may necessitate a 10–20% increase in expenditures to cover all eligible populations. Such substantial budgetary pressures challenge the traditional cost-effectiveness frameworks applied to routine oral medications, often failing to fully account for the indirect economic benefits of reduced relapse rates, diminished healthcare utilization, and improved long-term patient outcomes (Endara-Mina et al., 2026; Mahesh et al., 2018). Furthermore, the lack of standardized reimbursement pathways for the combined costs of both the medication itself and the associated provider-administered delivery creates a persistent barrier to entry, potentially exacerbating existing disparities in care access between well-resourced centers and resource-limited settings (Atif et al., 2025; Olagunju et al., 2025). Consequently, evolving reimbursement models—such as value-based contracting—remains critical to ensuring that the long-term clinical advantages of these therapies are both sustainable and equitably distributed across diverse populations (Tobias et al., 2023, p. 2449).

Beyond financial hurdles, the adoption of long-acting agents is frequently impeded by deep-seated clinical misconceptions, including the perception that such treatments should be reserved exclusively for later stages of disease progression rather than as proactive strategies for early-phase management. This clinical inertia often stems from a lack of provider familiarity with the unique pharmacokinetic profiles and long-term benefits of depot formulations, leading many to favor familiar daily oral regimens until standard therapies have already failed (Bajorek et al., 2025). Furthermore, when clinicians relegate injectable options to the role of 'rescue' therapies for refractory cases, they unintentionally forgo opportunities for early stabilization and the improved quality of life associated with enhanced, consistent adherence (Atif et al., 2025). Overcoming these deeply ingrained perspectives necessitates comprehensive clinician education that reframes long-acting therapeutics not as a last resort, but as a foundational tool for mitigating disease progression through reliable, sustained medication delivery (Gilroy et al., 2015, p. 171).

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Future Directions and Innovation

The evolution of long-acting therapeutics is poised to transition from static, pre-programmed depot formulations toward smart, closed-loop delivery systems that dynamically adjust dosage in response to real-time physiological feedback (Majji et al., 2025; S, 2025). These next-generation platforms will leverage AI-integrated sensors and biomarker-responsive biomaterials—such as hydrogels engineered to detect specific protein concentrations or pH fluctuations—to autonomously monitor systemic disease markers, enabling the precise, on-demand release of therapeutic agents precisely when needed (Aguado et al., 2018, p. 4; Cook & Decuzzi, 2021; Shigemitsu et al., 2020, p. 3860). By moving beyond the rigid, periodic dosing schedules inherent to current injectables, this paradigm shift toward personalized, precision-controlled drug administration promises to optimize therapeutic efficacy while inherently mitigating the risk of over- or under-exposure (Ali et al., 2024, p. 10; S, 2025). Ultimately, these intelligent systems, which can be further refined through machine learning algorithms to predict individual release kinetics, ensure that pharmacological interventions are perfectly synchronized with a patient's unique metabolic state and evolving disease progression (Majji et al., 2025; Park et al., 2024).

Emerging Therapeutic Platforms

Equally transformative is the emergence of encapsulated cell biofactories—genetically engineered allogeneic cells confined within semipermeable, immunoprotective membranes that reframe long-acting therapy from finite drug depots into continuously self-renewing biological production systems, sustaining *de novo* synthesis and release of therapeutic proteins for months to years after a single, retrievable implantation (Fliervoet & Mastrobattista, 2016; Grogg et al., 2023; Lathuilière et al., 2013).

Concurrently, mRNA-based platforms are being explored to direct in vivo protein expression, potentially bypassing the need for exogenous delivery by transforming the patient's own tissues into localized, sustained-release therapeutic hubs (Sawale et al., 2026). Furthermore, the integration of programmable, gene-based delivery systems offers the potential for clinicians to remotely modulate these internal bioreactors via external triggers, effectively merging gene therapy with precise, real-time dosing control (Pons-Faudoa et al., 2019, p. 66).

AUTHOR CONTRIBUTION

All the authors have played a significant role in their contribution.

CONFLICT OF INTEREST

There was no funding or conflict of interest related to this work.

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