

Long-Acting Injectable and Implantable Dosage Forms: A Paradigm Shift in Chronic Disease

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ABSTRACT

The global burden of chronic diseases such as diabetes, HIV, schizophrenia, and hormonal imbalances continues to grow, placing immense pressure on healthcare systems and patients alike. Traditional oral or short-acting parenteral therapies are often hindered by poor adherence, leading to suboptimal outcomes, resistance development, and increased morbidity. Long-acting injectable and implantable dosage forms offer a transformative approach to overcoming these limitations. By providing sustained therapeutic effects over extended periods, these delivery systems represent a significant advancement in chronic disease management. This review explores the principles, mechanisms, clinical applications, benefits, limitations, and future potential of these advanced drug delivery platforms.

KEYWORDS: Long-acting injectable, chronic diseases, Parenterals

INTRODUCTION

Chronic diseases such as diabetes, cardiovascular disorders, HIV/AIDS, mental health conditions, and autoimmune diseases necessitate lifelong pharmacological management.(1) The success of these therapies, however, is not solely determined by drug efficacy but also by the patient's ability and willingness to follow prescribed regimens consistently.(2) Unfortunately, adherence to daily medications is often poor, with reported nonadherence rates ranging from 30% to as high as 70% across various chronic conditions. This nonadherence can be attributed to a multitude of factors including complex dosing schedules, undesirable side effects, forgetfulness, psychological resistance to chronic medication use, and disruptions to daily routines. Moreover, in low-resource or rural settings, logistical challenges such as limited access to pharmacies, transportation issues, and inadequate patient education further exacerbate the problem.(3)

The consequences of poor adherence are profound. They include disease progression, increased risk of complications, higher hospitalization rates, reduced quality of life, and a significant financial burden on healthcare systems. For example, in diseases like HIV, inconsistent dosing can lead to the development of drug-resistant viral strains, while in conditions like schizophrenia, missed doses often result in relapse and re-hospitalization.(4)

To address these limitations, long-acting injectable (LAI) and implantable drug delivery systems have emerged as innovative

and practical alternatives. These advanced formulations are designed to release therapeutic agents slowly and continuously over a prolonged period, ranging from weeks to several months, and in some cases, up to a year. The pharmacological principle behind these systems involves sustaining consistent drug plasma concentrations, thereby avoiding the peaks and troughs associated with traditional dosing and minimizing both toxicity and subtherapeutic exposure.(5)

By significantly reducing the frequency of administration often to just once every few weeks or months these systems alleviate the daily responsibility placed on patients. This not only improves adherence but also leads to better disease control, reduced symptom fluctuations, and enhanced overall treatment satisfaction. Additionally, for healthcare providers, long-acting systems enable more structured monitoring of therapy and provide greater confidence that patients are receiving the intended dosage consistently. Ultimately, these technologies represent a shift from reactive, patient-dependent care to a more proactive, sustained therapeutic model, aligning pharmacotherapy more closely with the biological demands of chronic illness management.(6)

Advantages of Long-Acting Dosage Forms

One of the most compelling benefits of long-acting systems is the reduction in dosing frequency. Instead of taking medications daily or weekly, patients can receive a single injection or implant that provides consistent drug exposure for extended

periods. This reduces pill burden and improves adherence significantly, especially in populations with mental health issues, substance use disorders, or limited access to healthcare facilities. Furthermore, these systems minimize the risk of fluctuating plasma drug concentrations, which can lead to breakthrough symptoms or toxicity. Maintaining a steady-state drug level enhances efficacy and reduces the risk of side effects commonly associated with peak-and-trough plasma levels seen in oral medications.

For healthcare providers, long-acting forms offer better control over treatment regimens. They can verify compliance more reliably, manage fewer medication errors, and observe improved patient stability, especially in psychiatric and infectious disease settings.(7-8)

MECHANISMS OF ACTION AND DELIVERY TECHNOLOGIES

Long-acting injectables are typically administered intramuscularly or subcutaneously and may consist of drug-laden micro-particles, nanosuspensions, or depot formulations. Upon administration, the drug is released gradually through mechanisms such as diffusion through a polymer matrix, erosion of biodegradable carriers, or slow dissolution of drug crystals. These methods ensure a controlled and prolonged release profile that can last from a few weeks to several months.

Implantable systems are small, rod-shaped devices placed under the skin, often in the upper arm or abdomen. They are designed to release a precise amount of drug over time through diffusion or degradation. Depending on the material used, implants can be biodegradable, removing the need for surgical removal, or non-biodegradable, requiring minor outpatient procedures for removal or replacement. The device's composition and design are tailored to the drug's chemical nature and the desired release kinetics.(9-10)

Clinical Applications in Chronic Disease Management

Mental Health Disorders

In psychiatry, adherence to medication is notoriously poor due to lack of insight, stigma, and side effects. Long-acting injectables have revolutionized the treatment of conditions such as schizophrenia and bipolar disorder. Antipsychotic drugs in long-acting form, administered monthly or bi-monthly, significantly reduce relapse rates, hospitalizations, and improve overall functioning. These formulations ensure therapeutic coverage even if the patient disengages from regular care temporarily. (11)

Infectious Diseases

In the management of chronic infections like HIV, long-acting antiretroviral injectables have gained attention as a major advancement. Patients can now receive monthly or bimonthly injections that maintain viral suppression without the need for daily oral intake. This not only improves adherence but also reduces the stigma and psychological burden of carrying or taking pills daily. For conditions like tuberculosis, long-acting therapies are being explored to simplify multi-drug regimens and ensure completion of therapy, which is critical to preventing drug resistance.(12)

Endocrine Disorders and Women's Health

Implantable hormonal systems have long been used in contraception and hormone replacement therapy. These implants offer up to three years of pregnancy prevention with minimal user intervention. Similarly, in managing menopause or chronic conditions like endometriosis, hormonal implants provide steady therapeutic hormone levels without the inconvenience of regular administration.(13)

In diabetes management, long-acting insulin formulations are being investigated to provide steady basal insulin coverage. While not yet widely available in implantable form, research is ongoing into devices that could deliver insulin over weeks or months, reducing the burden of multiple daily injections.(14)

Pain Management

For opioid use disorder, long-acting buprenorphine implants provide continuous opioid receptor modulation, reducing cravings and preventing withdrawal symptoms. These implants support recovery by eliminating the need for daily medication and reducing the potential for diversion or misuse. In chronic pain management, long-acting local anesthetics or opioid implants can reduce dependence on systemic analgesics, improving patient safety.(15)

Limitations and Challenges

Despite their advantages, long-acting systems are not without drawbacks. The initial cost of these therapies is typically higher than traditional oral medications, which can limit accessibility, especially in low-income populations. Although the long-term cost-effectiveness may be favorable due to reduced hospitalizations and complications, upfront expenses remain a barrier.(16)

Implantation procedures, although minor, are invasive and may deter some patients. There is also a risk of site infections, in-

flammation, or device malfunction. Once administered, the drug cannot be easily removed or stopped, which poses challenges in case of adverse reactions or changes in therapy. In contrast to oral medications that can be stopped immediately, reversing the effects of a long-acting depot requires medical intervention.(9)

Patient-specific factors such as body weight, metabolism, and immune responses can also affect the performance of long-acting systems. Moreover, not all drugs are chemically stable or effective in long-acting formulations. Developing suitable candidates involves complex formulation science and regulatory pathways, increasing the time and cost required for market approval.(17)

FUTURE PERSPECTIVES

The future of long-acting delivery systems is promising. Researchers are developing “smart” implants that can respond to physiological signals or external triggers to release drugs on demand. Such systems could revolutionize care by offering not just sustained delivery but intelligent, adaptive therapy.(18)

Combination long-acting systems are also being explored, capable of delivering multiple drugs simultaneously for diseases that require polypharmacy. This would further streamline therapy for complex conditions such as HIV with co-infections or patients with multiple chronic diseases.(19)

Technological advances in biodegradable materials and miniaturization are likely to make implants safer, smaller, and easier to administer. Refillable implants and injectable microreservoirs are under development, potentially allowing years of treatment with minimal invasiveness.(20) Global health applications are especially promising. Long-acting injectables could reduce the burden on healthcare systems by minimizing the frequency of patient visits, which is particularly important in resource-limited settings. They also offer a more discreet option for patients concerned about stigma, especially in diseases like HIV or mental illness.(21)

7. Conclusion

Long-acting injectable and implantable dosage forms represent a significant evolution in the treatment of chronic diseases. By shifting the paradigm from daily management to long-term, sustained therapy, they address one of the most persistent barriers to effective care—adherence. Although challenges remain in terms of cost, drug selection, and implementation, the potential of these technologies to improve outcomes, enhance quality of life, and reduce healthcare burdens is immense. Continued

innovation, supported by policy and education, will be key to realizing their full promise in global healthcare.

REFERENCES

1. Dashputre NL, Laddha UD, Ahire ED, Bandawane DD, Patil SB, Kadam JD. Overview of Chronic Diseases. *Nov Drug Deliv Syst Manag Chronic Dis*. Apple Academic Press; 2024. p. 3–35.
2. Khunti K, Chudasama Y V, Gregg EW, Kamkuemah M, Misra S, Suls J, et al. Diabetes and multiple long-term conditions: a review of our current global health challenge. *Diabetes Care*. 2023;46:2092–101.
3. Konstantinou P, Kassianos AP, Georgiou G, Panayides A, Papageorgiou A, Almas I, et al. Barriers, facilitators, and interventions for medication adherence across chronic conditions with the highest non-adherence rates: a scoping review with recommendations for intervention development. *Transl Behav Med*. 2020;10:1390–8.
4. Vogeli C, Shields AE, Lee TA, Gibson TB, Marder WD, Weiss KB, et al. Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. *J Gen Intern Med*. 2007;22:391–5.
5. Bauer A, Berben P, Chakravarthi SS, Chatterraj S, Garg A, Gourdon B, et al. Current state and opportunities with long-acting injectables: industry perspectives from the innovation and quality consortium “long-acting injectables” working group. *Pharm Res*. 2023;40:1601–31.
6. Benjamin DM. Reducing medication errors and increasing patient safety: case studies in clinical pharmacology. *J Clin Pharmacol*. 2003;43:768–83.
7. McEvoy JP. Risks versus benefits of different types of long-acting injectable antipsychotics. *J Clin Psychiatry*. 2006;67:15–
8. Altreuter DH, Kirtane AR, Grant T, Kruger C, Traverso G, Bellinger AM. Changing the pill: developments toward the promise of an ultra-long-acting gastroretentive dosage form. *Expert Opin Drug Deliv*. 2018;15:1189–98.
9. Owen A, Rannard S. Strengths, weaknesses, opportunities and challenges for long acting injectable therapies: Insights for applications in HIV therapy. *Adv Drug Deliv Rev*. 2016;103:144–56.
10. Kim Y-C, Min KA, Jang D-J, Ahn TY, Min JH, Yu BE, et al. Practical approaches on the long-acting injections.

- J Pharm Investig. 2020;50:147–57.
11. Llorca PM, Abbar M, Courtet P, Guillaume S, Lancrenon S, Samalin L. Guidelines for the use and management of long-acting injectable antipsychotics in serious mental illness. *BMC Psychiatry*. 2013;13:1–17.
 12. Flexner C, Owen A, Siccardi M, Swindells S. Long-acting drugs and formulations for the treatment and prevention of HIV infection. *Int J Antimicrob Agents*. 2021;57:106220.
 13. Kaunitz AM. Injectable long-acting contraceptives. *Clin Obstet Gynecol*. 2001;44:73–91.
 14. Davis CS, Fleming JW, Malinowski SS, Brown MA, Fleming LW. Ultra-long-acting insulins: a review of efficacy, safety, and implications for practice. *J Am Assoc Nurse Pract*. 2018;30:373–80.
 15. O'Brien MN, Jiang W, Wang Y, Loffredo DM. Challenges and opportunities in the development of complex generic long-acting injectable drug products. *J Control Release*. 2021;336:144–58.
 16. Gonella A, Grizot S, Liu F, López Noriega A, Richard J. Long-acting injectable formulation technologies: challenges and opportunities for the delivery of fragile molecules. *Expert Opin Drug Deliv*. 2022;19:927–44.
 17. Alidori S, Subramanian R, Holm R. Patient-centric long-acting injectable and implantable Platforms— An industrial perspective. *Mol Pharm*. 2024;21:4238–58.
 18. Bassand C, Villos A, Gianola L, Laue G, Ramazani F, Riebeschl B, et al. Smart design of patient-centric long-acting products: from preclinical to marketed pipeline trends and opportunities. *Expert Opin Drug Deliv*. 2022;19:1265–83.
 19. Jindal AB, Bhide AR, Salave S, Rana D, Benival D. Long-acting parenteral drug delivery systems for the treatment of chronic diseases. *Adv Drug Deliv Rev*. 2023;198:114862.
 20. Stevenson CL, Santini Jr JT, Langer R. Reservoir-based drug delivery systems utilizing microtechnology. *Adv Drug Deliv Rev*. 2012;64:1590–602.
 21. Rathore G, Singh RP. Transforming Disease Management: The Clinical Benefits of Long-Acting Injectable Drug Delivery Systems. *Intell Hosp*. 2025;100001.