

Current Trends in Osmotic Pump Drug Delivery Systems



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Abstract: Traditional oral drug delivery methods, which typically release medication immediately, often lead to fluctuations in plasma drug concentration, potentially causing suboptimal therapeutic outcomes and side effects. Osmotic pump drug delivery systems address these issues by providing a controlled release mechanism that ensures a steady and predictable release of the drug over an extended period. This controlled release enhances patient compliance by reducing the frequency of dosing and maintaining uniform blood concentration levels, thereby improving therapeutic efficacy. Unlike conventional drug delivery methods, osmotic pumps are less influenced by physiological variables within the gastrointestinal tract, making them a reliable and consistent option for controlled drug delivery. These systems operate on the principles of osmosis, utilizing a semipermeable membrane to regulate the influx of water into the drug-containing core, which then generates osmotic pressure to drive the drug out through a delivery orifice. This review provides an in-depth discussion of the principles behind osmotic drug delivery systems, the various types available, their benefits, and the challenges they present. It also highlights the significance of these systems in modern pharmaceutical applications, demonstrating how they represent a significant advancement over traditional methods by optimizing drug release profiles, improving patient adherence, and ultimately enhancing therapeutic outcomes.

Keywords: Novel drug delivery system, Osmosis; Osmotic drug delivery system, Osmotic pumps.

1. Introduction

The field of drug delivery has evolved significantly over the past few decades, driven by the need to enhance the efficacy of therapeutic agents while minimizing side effects and improving patient compliance. Traditional oral drug delivery methods, characterized by immediate release formulations, often result in significant fluctuations in plasma drug concentrations. These fluctuations can lead to periods of subtherapeutic levels or toxic peaks, which can compromise the overall therapeutic efficacy and increase the risk of adverse effects. To address these limitations, various controlled release systems have been developed, among which osmotic pump drug delivery systems have garnered considerable attention due to their ability to provide a steady and controlled release of medication. Osmotic pump drug delivery systems operate on the fundamental principles of osmosis. Osmosis is the movement of water molecules through a semipermeable membrane from a region of lower solute concentration to a region of higher solute concentration. In the context of drug delivery, these systems typically consist of a core containing the active pharmaceutical ingredient (API) and osmotically active agents, surrounded by a semipermeable membrane. When the system is exposed to bodily fluids, water permeates through the membrane, dissolving the osmotically active agents and creating osmotic pressure. [1] This pressure drives the drug solution out through a delivery orifice, allowing for a controlled and sustained release of the medication.

Several types of osmotic pump systems have been developed to cater to different therapeutic needs and drug properties. The Elementary Osmotic Pump (EOP), one of the simplest forms, consists of a tablet core coated with a semipermeable membrane and a small orifice for drug release. The Push-Pull Osmotic Pump (PPOP) is designed for drugs with varying solubility and features a bilayer tablet core, one layer containing the drug and the other containing an osmotic agent. [2] The Controlled Porosity Osmotic Pump (CPOP) includes a core with water-soluble additives and an asymmetric membrane that forms micropores for drug release. Each of these systems leverages the principles of osmosis to achieve a zero-order release rate, ensuring a consistent delivery of the drug over time.

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Osmotic pump drug delivery systems offer several advantages over traditional and other controlled release systems. One of the primary benefits is the ability to maintain a consistent plasma drug concentration, which enhances therapeutic efficacy and reduces the risk of side effects associated with fluctuating drug levels. These systems also improve patient compliance by reducing the frequency of dosing. Additionally, osmotic pumps are less influenced by the physiological variables within the gastrointestinal tract, such as pH and motility, making them a more reliable option for controlled drug delivery. The predictability of drug release from osmotic pumps is another significant advantage, as it allows for better tailoring of dosage regimens to meet individual patient needs. Despite their numerous benefits, osmotic pump drug delivery systems also present certain challenges. The design and manufacturing of these systems are more complex compared to traditional dosage forms, requiring precise control over the properties of the semipermeable membrane and the formulation of the core. Additionally, the cost of production can be higher, which may affect the affordability of these systems. [3] There are also considerations related to the drug's solubility and stability within the osmotic system, as well as the potential for dose dumping if the system fails. Addressing these challenges requires ongoing research and development to optimize the formulation and manufacturing processes. The development of osmotic pump drug delivery systems represents a significant advancement in pharmaceutical technology. These systems offer a superior alternative to traditional drug delivery methods by optimizing drug release profiles, improving patient adherence, and ultimately enhancing therapeutic outcomes. Their ability to provide consistent and controlled drug delivery makes them particularly valuable for the treatment.

2. Background

2.1. Osmosis and its principle

Osmosis refers to the movement of solvent molecules through a semipermeable membrane from an area of lower solute concentration to one of higher concentration. This process is driven by osmotic pressure, which is a colligative property dependent on solute concentration. An osmotic drug delivery system leverages this principle to regulate the influx of water and subsequently release the drug at a controlled rate. [4] In an osmotic drug delivery system, the drug is combined with osmotically active agents in a core surrounded by a semipermeable membrane. When water permeates through the membrane, it dissolves the osmotically active agents, creating pressure that drives the drug solution out through a delivery orifice. This results in a zero-order release rate, ensuring a consistent delivery of the drug over time [5]

2.2. Types of osmotic pumps

Types of osmotic pumps are shown in Figure 1.

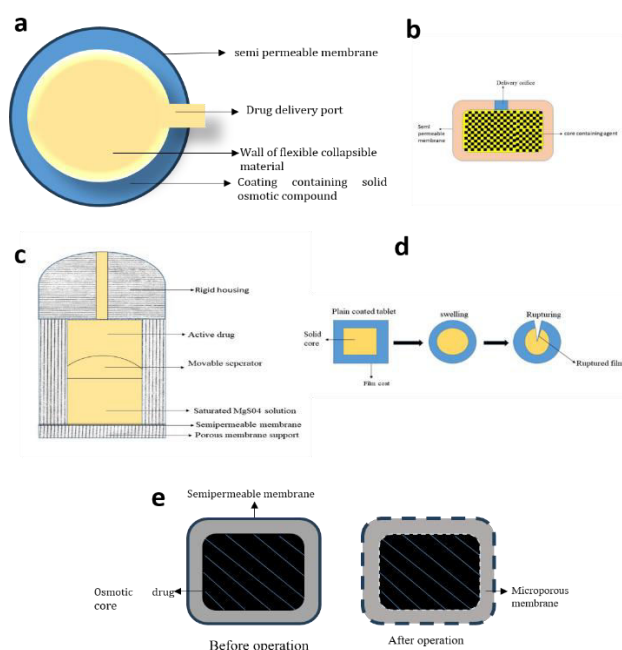


Figure 1. Types of osmotic pumps a. Higuchi-Theeuwes pump b. Higuchi Loper pump c. Elementary osmotic pump d. Controlled porosity osmotic pump e. Bursting type osmotic pump

2.2.1. Elementary Osmotic Pump (EOP)

The Elementary Osmotic Pump, developed by Theeuwes in 1974, is a simple yet effective system comprising a tablet core coated with a semipermeable membrane, typically cellulose acetate. A small orifice is drilled in the membrane to allow the drug solution to be released at a controlled rate. [5]

2.2.2. Push-Pull Osmotic Pump

This system is designed to deliver drugs with varying solubility. It consists of a bilayer tablet core with one layer containing the drug and the other containing an osmotic agent. Upon ingestion, water is absorbed, creating pressure that pushes the drug layer through the delivery orifice. [5]

2.2.3. Controlled Porosity Osmotic Pump

Introduced by Zenter in 1985, this system features a core with the drug and water-soluble additives, surrounded by an asymmetric membrane. The membrane allows selective permeability of water, forming micropores through which the drug is released. [5]

2.2.4. Rose-Nelson Pump

Developed in 1955, this is the first implantable osmotic pump, designed for veterinary use. It comprises an elastic diaphragm and a semipermeable membrane, which creates an osmotic pressure gradient that drives the medication out of the device. [5]

2.2.5. Higuchi-Leeper Pump

This pump, a modification of the Rose-Nelson design, includes a rigid casing, a semipermeable membrane, and a salt chamber. The osmotic pressure created drives the drug solution through a delivery port. [5]

2.2.6. Monolithic Osmotic Systems

These systems incorporate the drug within a polymer matrix. Upon contact with water, the polymer swells and ruptures, releasing the drug at a controlled rate. [5]

2.2.7. Osmotic Bursting Pumps

Designed by Baker, these pumps may lack a delivery orifice or have a very small one. The osmotic pressure causes the device to burst, releasing the drug in a pulsed manner. [5]

2.2.8. Asymmetrical Membrane Osmotic Tablets

These devices consist of an asymmetric membrane surrounding a core loaded with the drug. The membrane selectively allows water to enter, gradually releasing the drug. [5]

2.2.9. Telescopic Capsule for Delayed Release

This system includes two chambers: one containing the drug and the other an osmotic engine. A wax-like layer separates the chambers. Upon activation, the osmotic pressure drives the drug out. [5]

3. Classification of osmotic pumps

The classification of osmotic pumps is shown in Figure 1.

3.1. Based on Activation Mechanism

- Osmotic Pressure-Activated Drug Delivery System: Utilizes the osmotic pressure gradient to drive drug release.
- Hydrodynamic Pressure-Activated Drug Delivery System: Uses hydrodynamic pressure changes within the body to control drug release.
- Vapour Pressure-Activated Drug Delivery System: Employs vapour pressure differences to facilitate drug delivery.
- Mechanically Activated Drug Delivery System: Mechanical forces trigger the release of the drug.
- Magnetically Activated Drug Delivery System: Uses magnetic fields to control drug release.
- Sonophoresis Activated Drug Delivery System: Ultrasonic waves facilitate drug delivery through the skin.
- Iontophoresis Activated Drug Delivery System: Electric currents drive drug molecules across membranes.
- Hydration Activated Drug Delivery System: Water absorption triggers drug release. [6]

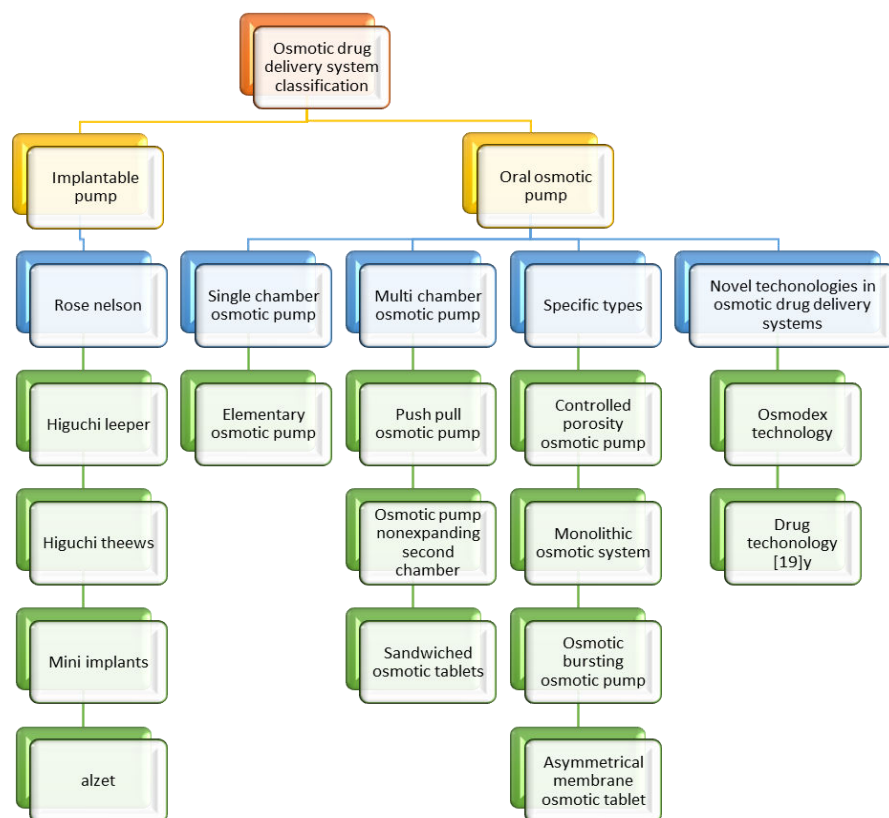


Figure 1. Classification of osmotic pumps

3.2. Based on activation means

- pH-Activated Drug Delivery System: Drug release is controlled by the pH of the surrounding environment.
- Ion Exchange Drug Delivery System: Utilizes ion exchange mechanisms to release the drug.
- Hydrolysis-Activated Drug Delivery System: Drug release is triggered by hydrolysis reactions
- Enzyme-Activated Drug Delivery System: Enzymatic reactions control the release rate of the drug.
- Biochemical Activated Drug Delivery System: Biochemical signals trigger drug release. [7]

4. Specific osmotic pump systems

4.1. Rose–Nelson Pump

The Rose–Nelson pump was the first implantable osmotic pump developed in 1955 for veterinary use. It consists of a water chamber and a semi-permeable membrane surrounding an elastic diaphragm. The osmotic pressure difference between the chambers causes water to flow into the salt chamber, expanding it and pushing the drug out of the device. [8]

4.2. Higuchi Theeuwes Pump

This pump features a semipermeable membrane and a rigid housing. The drug is placed in the device, and its release is controlled by the permeability of the outer membrane and the osmotic agents in the salt chamber. The delivery port is designed to minimize diffusional loss. [9]

4.3. Higuchi Leeper Pump

A variant of the Rose–Nelson pump, the Higuchi Leeper pump has a rigid casing, a semipermeable membrane on a perforated frame, and no water chamber. It typically contains a salt chamber with excess solid salt in a fluid solution, ensuring consistent drug release. [10]

4.4. Oral Osmotic Pumps

4.4.1. Single Chamber Osmotic Pump-Elementary Osmotic Pump (EOP)

Simplified from the Rose–Nelson pump, the EOP consists of a tablet coated with a semipermeable membrane, often cellulose acetate. A small orifice allows the drug solution to be released at a controlled rate. [11]

4.4.2. Multi-Chamber Osmotic Pump

- **Push-Pull Osmotic Pump:** Designed for drugs with varying solubility, this system has a bi-layer tablet core with osmotic agents in one layer and the drug in the other. Water absorption creates pressure, pushing the drug layer through the delivery orifice.
- **Osmotic Pump with Non-Expanding Second Chamber:** This multi-compartment device includes a non-expanding chamber that dilutes the drug solution before release, reducing gastrointestinal irritation.
- **Sandwiched Osmotic Tablet:** Features a core with the drug sandwiched between two osmotic layers, all surrounded by a semipermeable membrane. Water absorption creates pressure from both osmotic layers, ensuring consistent drug release.

5. Current Trends in Osmotic Pumps

Osmotic pump drug delivery systems have significantly evolved since their inception, driven by technological advancements and increasing demand for more effective and patient-friendly medication delivery methods. Recent trends in osmotic pump technology focus on enhancing the efficiency, versatility, and applicability of these systems. Key areas of innovation include the development of new materials, advanced manufacturing techniques, integration with smart technologies, and the exploration of novel therapeutic applications. [12]

5.1. Advances in Materials and Membrane Technology

One of the most critical components of osmotic pumps is the semipermeable membrane, which regulates the influx of water and controls the drug release rate. Recent research has focused on developing advanced materials that offer improved permeability and mechanical properties. Innovations in polymer science have led to the creation of membranes with enhanced biocompatibility, reduced toxicity, and greater stability under physiological conditions. [13] For instance, the use of biodegradable polymers like poly(lactic-co-glycolic acid) (PLGA) offers the dual benefit of controlled drug release and gradual degradation within the body, eliminating the need for surgical removal of the delivery device. Additionally, the incorporation of nanotechnology into membrane design has enabled the development of membranes with nanoscale pores, providing more precise control over drug release rates. [14]

5.2. Smart Osmotic Pumps

The integration of smart technology into osmotic pumps represents a significant trend aimed at improving the adaptability and functionality of these systems. Smart osmotic pumps are designed to respond to physiological signals or external triggers, allowing for more personalized and dynamic drug delivery. [15] These systems can incorporate sensors to monitor biological parameters such as pH, glucose levels, or temperature, adjusting the drug release rate in real-time based on the detected conditions. Moreover, the use of wireless communication technologies enables remote control and monitoring of drug delivery, providing healthcare professionals with the ability to tailor treatment regimens more precisely. [16] This capability is particularly beneficial for managing chronic conditions where drug requirements can vary significantly over time.

5.3. Microfabrication and Miniaturization

Microfabrication techniques have revolutionized the design and manufacturing of osmotic pumps, leading to the development of miniaturized devices that can be implanted or ingested more easily. [17] Microelectromechanical systems (MEMS) technology, for example, allows for the precise fabrication of microscale components, enhancing the performance and reliability of osmotic pumps. Miniaturized osmotic pumps are particularly advantageous for pediatric and geriatric patients, as well as for applications requiring localized drug delivery, such as in the treatment of eye diseases or targeted cancer therapy. These smaller devices can provide controlled drug release while minimizing discomfort and improving patient compliance. [18]

5.4. Personalized Medicine and Targeted Delivery

The trend towards personalized medicine has spurred the development of osmotic pumps that can be tailored to individual patient needs. By customizing the drug formulation, release profile, and device design, these systems can provide more effective and patient-specific treatments. This approach is particularly relevant for conditions requiring long-term medication, such as diabetes, hypertension, and neurological disorders. Targeted drug delivery is another emerging trend, where osmotic pumps are

designed to deliver drugs directly to specific tissues or organs, thereby maximizing therapeutic efficacy while minimizing systemic side effects. Techniques such as magnetically guided delivery, where magnetic nanoparticles are incorporated into the drug formulation and directed to the target site using an external magnetic field, exemplify this trend. [19]

5.5. Combination Therapies

Combining multiple therapeutic agents within a single osmotic pump is a growing trend aimed at enhancing treatment efficacy and reducing the complexity of medication regimens. These combination therapies can address multiple aspects of a disease simultaneously, offering a more comprehensive treatment approach. For example, in cancer therapy, an osmotic pump could deliver both chemotherapeutic agents and drugs that mitigate side effects, improving patient outcomes and quality of life. [20]

5.6. Regulatory and Manufacturing Challenges

The advancement of osmotic pump technology also brings regulatory and manufacturing challenges that need to be addressed. Ensuring the safety, efficacy, and quality of these systems requires rigorous testing and validation processes. Regulatory agencies are developing guidelines to facilitate the approval of novel osmotic pump designs, focusing on aspects such as biocompatibility, drug stability, and release kinetics. Manufacturing these advanced systems involves sophisticated techniques that can be costly and time-consuming. However, innovations in manufacturing processes, such as 3D printing and automated assembly, are helping to streamline production and reduce costs, making these advanced drug delivery systems more accessible. [21]

5.7. Future directions

The future of osmotic pump drug delivery systems is poised to benefit from several emerging trends and technological advancements. [22] Here are some key areas that are likely to shape the next generation of these systems:

5.7.1. Integration with Digital Health Technologies

The integration of osmotic pumps with digital health technologies is a promising trend. Wearable devices and mobile health applications can be used to monitor patients' vital signs and other health parameters in real time. By combining this data with osmotic pumps, it is possible to create smart drug delivery systems that can adjust dosages automatically based on the patient's current condition. [23] This approach can lead to more personalized and effective treatments.

5.7.2. 3D Printing and Customizable Designs

3D printing technology offers the potential to create highly customizable osmotic pump systems tailored to the specific needs of individual patients. This includes the ability to design pumps with unique shapes and sizes that fit precisely within the patient's body, as well as the ability to incorporate multiple drugs with different release profiles into a single device. Customizable designs can enhance the effectiveness of treatment and improve patient comfort and compliance. [24]

5.7.3. Biodegradable and Eco-Friendly Materials

There is a growing interest in developing osmotic pumps from biodegradable and eco-friendly materials. These materials can reduce the environmental impact of medical waste and eliminate the need for surgical removal of the device after the drug has been fully delivered. Research into biopolymers and other sustainable materials is ongoing, with the goal of creating safe and effective biodegradable osmotic pumps.

5.7.4. Combination with Advanced Drug Formulations

Combining osmotic pump technology with advanced drug formulations, such as nanoparticles, liposomes, and biologics, can enhance the delivery and efficacy of these therapeutic agents. These formulations can improve the solubility, stability, and bioavailability of drugs, allowing for more precise and controlled delivery. This combination is particularly useful for the delivery of complex biologics like monoclonal antibodies and gene therapies. [25]

5.7.5. Enhanced Targeting and Site-Specific Delivery

Future osmotic pump systems are likely to incorporate advanced targeting mechanisms to deliver drugs more precisely to specific tissues or organs. Techniques such as magnetically guided delivery, ultrasound-mediated targeting, and ligand-receptor interactions can be used to direct the drug to the desired site within the body. This approach can maximize therapeutic efficacy while minimizing systemic exposure and side effects.

5.7.6. Regulatory and Ethical Considerations

As osmotic pump technology continues to advance, regulatory and ethical considerations will play a crucial role in its development and implementation. Ensuring the safety, efficacy, and quality of these systems will require adherence to rigorous regulatory

standards and guidelines. Additionally, ethical considerations related to patient consent, data privacy, and the equitable distribution of advanced drug delivery technologies will need to be addressed. [26]

6. Conclusion

Osmotic pump drug delivery systems have proven to be a robust and reliable method for achieving controlled and sustained drug release. Their ability to maintain consistent plasma drug concentrations significantly enhances therapeutic efficacy and patient compliance. By utilizing the principles of osmosis, these systems are largely unaffected by gastrointestinal variables, ensuring predictable and uniform drug delivery. The versatility of osmotic pumps, applicable to both oral and implantable routes, further expands their utility in various therapeutic areas. Despite their complexity, advancements in formulation and manufacturing techniques continue to improve their feasibility and cost-effectiveness. Overall, osmotic pumps represent a critical innovation in pharmaceutical technology, offering a superior alternative to traditional drug delivery methods.

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