doi.org/10.36721/PJPS.2026.39.7.181.1

REVIEW

Oral osmotic pump drug delivery systems: A narrative review of structural designs, functional mechanisms and emerging applications

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Abstract: Traditional oral formulations often lead to significant fluctuations in plasma drug concentrations. In contrast, oral osmotic pumps achieve zero-order drug release driven by osmotic pressure, which is largely independent of physiological variables, offering an effective solution to optimize drug delivery outcomes. This review aims to summarize the structural types, functional mechanisms, and key factors influencing drug release of oral osmotic pumps, compare their performance disparities, and provide valuable references for subsequent research and development in this field. Oral osmotic pump systems were classified based on their structural designs, their mechanisms of action and key drug release-influencing factors were elaborated, and the characteristics and application potential of different systems were comparatively evaluated. Oral osmotic pump systems can be categorized into single-chamber, multi-chamber, and specific types, with push-pull osmotic pumps particularly suitable for poorly soluble drugs and targeted systems enabling site-specific therapy. Drug properties, osmotic pressure, semipermeable membrane characteristics, and release orifice parameters are critical factors governing drug release. Despite advantages such as stable release profiles and broad applicability, the system is limited by complex preparation processes and high costs. Oral osmotic pumps represent a highly valuable drug delivery technology. Future integration with intelligent technologies and advanced materials is expected to overcome existing challenges, facilitating more precise and efficient drug delivery.

Keywords: Oral osmotic pump; Osmotic pressure; Semipermeable membrane

Submitted on 11-10-2025 – Revised on 18-11-2025 – Accepted on 01-12-2025

INTRODUCTION

Oral medications, the most favored route of drug delivery, offer several advantages, including convenience, cost-effectiveness and patient compliance (Talukdar and Shivakumar, 2023). Traditional oral formulations, such as tablets and capsules, have served as the foundation of drug therapy for a considerable time due to their simple manufacturing process, stability and ease of administration (Snehal *et al*., 2023). However, these formulations frequently result in considerable fluctuations in plasma drug concentrations, leading to erratic therapeutic effects, toxicity, or ineffectiveness (Zhao *et al.*, 2015). These shortcomings stem primarily from the limitations of traditional dosage forms, including the inability to control drug release rates and the influence of physiological factors (such as gastric emptying time and intestinal pH) on drug absorption (Radice *et al*., 2022). There is a growing need for advanced drug delivery systems. These systems are required to address current issues and provide more consistent and predictable therapeutic outcomes (Losada-Barreiro *et al*., 2024). To address these constraints, innovative drug delivery methods, especially those involving sustained and controlled release, have become the focus of extensive research and patent filings, suggesting their potential as viable alternatives (Chen *et al*., 2024). These systems are designed to modulate drug release kinetics, improve efficacy, minimize side effects and enhance patient compliance (Patel and Parikh, 2017). Among these, osmotic pump delivery systems (shown in Table 1) stand out for their unique zero-order drug release capability, which is largely independent of factors such as pH and gastrointestinal (GI) motility (Almoshari, 2022). Osmotic pumps utilize osmosis to generate a constant driving force for drug release, thus maintaining stable plasma drug concentrations over extended periods.

Osmotic pumps control drug delivery through osmotic pressure (Mansour *et al*., 2023; Liu *et al*., 2025). Their core components comprise a semi-permeable membrane (SPM), an osmotic agent and a drug-containing core (Shah and Makwana, 2021; Wang *et al*., 2008). The SPM allows water influx while blocking the movement of drugs and dissolved substances (Brighenti and Cosma, 2020), establishing an osmotic pressure gradient (Li *et al*., 2021). Dissolution of the osmotic agent within the pump generates

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high osmotic pressure, attracting external water and increasing internal pressure (Ning *et al*., 2011; Wu *et al*., 2014). As water continuously enters, the drug, whether in solution, suspension, or emulsion form, is subjected to a constant force, propelling it steadily through the release orifice. This achieves zero-order drug release, guaranteeing stable drug delivery in the body (Sahoo *et al*., 2015; Farooqi *et al*., 2020). The evolution of osmotic pump technology represents a process of continuous innovation, with each generation addressing the limitations of its predecessor (Dasankoppa *et al*., 2012). Pharmaceutical formulators have consistently innovated in structural designs, from elementary single-chamber systems to sophisticated multichamber configurations and in materials science to enhance performance and expand applications (Li *et al*., 2016; Liu *et al*., 2014; Maharjan *et al*., 2022). These incremental yet critical advancements have established a robust technological foundation. The recent emergence of novel concepts, such as intelligent formulations and advanced manufacturing techniques, builds directly upon this deep understanding of fundamental osmotic pump principles (Chen *et al*., 2024; Saleem *et al*., 2025; Navarro-Tumar *et al*., 2024).

Based on the method of administration, osmotic pump drug delivery systems fall into two main categories: implantable and oral (Ogueri and Shamblin, 2022; Chen *et al*., 2024). This review focuses specifically on oral osmotic pumps. Accordingly, this review aims to provide a detailed examination of well-established oral osmotic pump systems. It will comprehensively classify their structural designs (including single chamber, multichamber and specific types), elucidate their core functional mechanisms and present a comparative analysis of their performance. Furthermore, the key factors governing drug release, such as drug properties and semi-permeable membrane design, are critically analyzed. By consolidating this essential knowledge, this work seeks to offer a clear architectural framework and a reliable theoretical basis, which are indispensable for the future development and rational design of next-generation osmotic pump systems.

Thematic sections

Mechanism

Utilizing SPM technology and osmosis principles, the osmotic pump drug delivery system ensures consistent and dependable drug release (El-Zahaby *et al*., 2018). The fundamental mechanism involves the drug core's high osmotic pressure, which effectively draws water from bodily fluids into the device through the SPM (Tian *et al*., 2016; Xu *et al*., 2013). The continuous influx of water leads to pressure accumulation within the device, subsequently driving the drug out of the core through the designated release orifice (Xue *et al*., 2015). The optimal osmotic pump functions based on zero-order release kinetics, wherein the drug is released at a steady, time-independent rate (Xie *et al*., 2016). This stability is attained by carefully controlling the SPM's characteristics and the osmotic agent's concentration in the core (Cheng *et al*., 2018). The rate (Li *et al*., 2004) of drug release (dM/dt) can be expressed as the product of the volumetric flux of water through the SPM (dv/dt) and the drug's concentration (C), as shown in Eq. (1):

$$\frac{dM}{dt} = \frac{dv}{dt} \times C \quad (1)$$

For a single-chamber osmotic pump tablet, the rate at which water passes through the SPM into the drug core can be expressed by Eq.(2):

$$\frac{dv}{dt} = \frac{KA}{L}\left(\mathrm{D}p - \mathrm{DR}\right) \quad (2)$$

In Eq.(2), K represents the permeability coefficient of the membrane to water, A and L denote the area and thickness of the SPM, respectively. Dp and DR indicate the osmotic pressure difference between the membrane's interior and exterior and the hydrostatic pressure difference (Atef and Belmonte, 2008; Song *et al*., 2022). Considering that the osmotic pump's internal osmotic pressure is significantly higher than that in the surrounding environment and provided that the release orifice is appropriately sized, the value of DR is minimal, $D_p \gg DR$ .Thus, Eq.(2) simplifies to Eq.(3):

$$\frac{dM}{dt} = \frac{KA}{L} \times Dp \times C \quad (3)$$

In Eq. (3), the properties of SPM determine the values of K, A and L. Conversely, the osmotic pressure difference (D_p) and drug concentration (C) depend on the state of the drug solution within the pump (Liu *et al*., 2014). Therefore, if the characteristics of SPM remain constant, the osmotic agent maintains a consistent high osmotic pressure difference, keeping the drug solution saturated (Ouyang *et al*., 2005). Under these conditions, the osmotic pump tablet achieves constant zero-order drug release. As the drug is fully dissolved, the concentration within the core progressively decreases, leading to a decline in the drug release rate until it ceases (Emara *et al*., 2014).

Oral-osmotic drug delivery devices

Single-chamber osmotic systems

Elementary osmotic pump (EOP)

The EOP (Fig. 1) originated in the 1970s and was patented by Theeuwes (Theeuwes, 1975). This device, which combined the osmotic principle with SPM technology, formed the basis for the subsequent development of oral osmotic pumps. Its primary components are the tablet core and a coating membrane. The tablet core comprises the drug and osmotic agent that generates significant osmotic pressure to enable drug release (Zhang *et al*., 2016). The coating membrane is composed of a polymer material, such as cellulose acetate and is semi-permeable, allowing water molecules to pass through while preventing the passage of drug molecules. A critical feature of the membrane is the inclusion of a release orifice, the size of which is precisely controlled to facilitate drug exit (Missaghi *et al*., 2013).

Table 1: Advantages and disadvantages of oral osmotic delivery systems

Advantages	Disadvantages
The product is suitable for use with multiple drug classes, including those with poor solubility and those requiring specific release profiles. It has a broad range of potential applications.	This approach may cause the drug in solution to decompose or polymerize; hence, it is not appropriate for medications having an unstable solution state.
The drug release demonstrates a zero-order profile, indicating independence from drug concentration.	Individual patient differences, including abnormal GI motility, may influence the drug release rate.
These systems have been shown to decrease variability in blood concentration and the occurrence of adverse effects.	The preparation process is inherently complex and costly.
The rate of drug release is independent of physiological conditions such as GI pH, enzymes, GI motility, and food intake. This minimizes variability among patients.	The preparation of the coating film and the perforation process necessitate the utilisation of precision instruments, the calibration of which is of paramount importance.
Reducing the frequency of drug administration can lead to improved patient compliance and enhanced quality of life for patients.	Insufficient control of the coating process may result in the formation of defects in the coating film, which can subsequently lead to dose dumping.
The amount of drug released can be predicted and designed, demonstrating substantial *in-vivo in-vitro* correlation.	In the case of complex preparations or special medication needs, patients require guidance from a professional to ensure the correct use of the medication.
It can be formulated into a delayed-release or pulsed preparation, as required.	
Individualized treatment based on the patient's medication needs.	

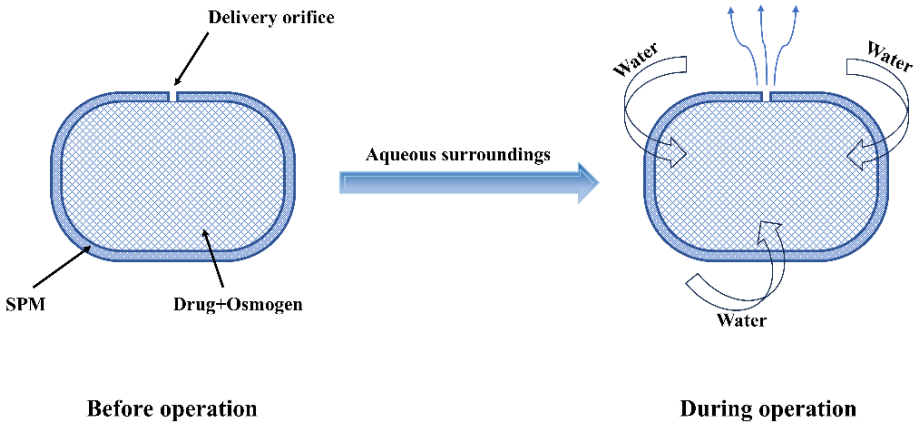

Fig. 1: Schematic diagram of the drug-release process in an EOP tablet with a single orifice.

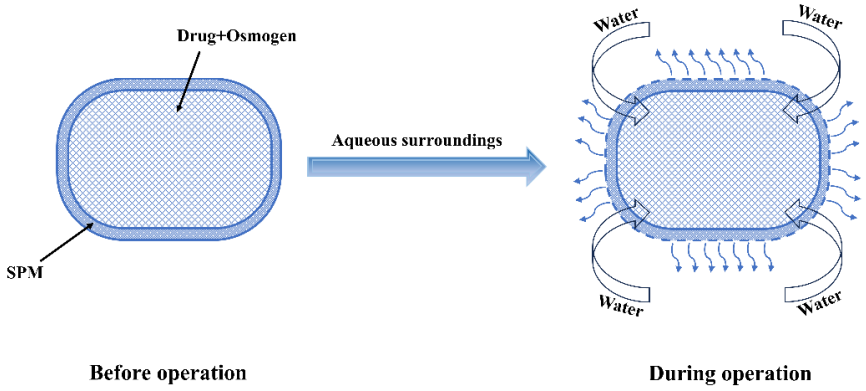

Fig. 2 Schematic diagram of the drug-release process in a CPOP tablet.

Osmotic agents, such as lactose and fructose, can be utilized to modulate the osmotic pressure in the drug chamber, facilitating sustained drug release (Patel *et al*., 2012). EOP can achieve zero-order drug release, largely independent of the GI tract's physiological conditions, thus ensuring a stable therapeutic effect and minimizing side effects (Kumaravelrajan *et al*., 2011). Furthermore, its simple design facilitates industrial production.

Controlled-porosity osmotic pump (CPOP)

CPOP (Fig. 2) still includes a drug core and an SPM, but its defining feature is the use of a pore-forming agent (Cheng *et al*., 2017). These agents are mostly hydrophilic and include substances such as polyvinylpyrrolidone, polyethylene glycol (PEG), or other soluble inorganic salts that dissolve upon contact with an aqueous environment, leaving precisely controlled pores for drug release (Bi *et al*., 2007; Chauhan and Choudhury, 2006). In addition to the pore-forming agent, the system may also contain osmotic agents such as lactose or fructose to maintain the osmotic pressure inside the drug chamber (Banerjee *et al*., 2014). CPOP eliminates the need for sophisticated perforating machines or drug layer identification techniques (Adibkia *et al*., 2013). The selection of suitable pore-forming agents and dosage adjustments enable precise control over the drug release rates, accommodating various treatment requirements while reducing burst release and enhancing medication safety (Patel *et al*., 2013; Song *et al*., 2012).

Single composition osmotic pump (SCOP)

SCOP tablets facilitate the controlled release of drugs through a straightforward preparation process. The composition comprises a drug-containing core and an SPM encapsulating the core, obviating the need for a push layer and thereby simplifying formulation complexity. Common excipients include osmotic agents (e.g., sodium chloride or sugars) to generate osmotic pressure and film-forming materials (e.g., cellulose acetate) (Pravinkumar Darji *et al*., 2024). The selection of these excipients must satisfy criteria for drug release characteristics and membrane stability. SCOP tablets are appropriate for water-soluble drugs at moderate doses, offering straightforward preparation, cost-effectiveness and consistent drug release rates (Xie *et al*., 2016). However, their applicability is constrained for poorly soluble drugs or those requiring high-dose delivery.

Multichambered osmotic systems

Push-pull osmotic pump (PPOP)

To address the need for controlled release of poorly soluble drugs, researchers have developed PPOP, a bilayer osmotic pump system (Hu *et al*., 2024). This system (Fig. 3) consists of a double-layered tablet core comprising a drug-containing layer and a push layer, encased within an outer SPM (Lin *et al*., 2022). The drug-containing layer incorporates the active pharmaceutical ingredient (API), while the push layer comprises osmotic agents capable of generating osmotic pressure. Common components include polymeric materials (e.g., polyethylene oxide (PEO), hydroxypropyl methylcellulose) and osmotically active substances (e.g., sodium chloride). These excipients must meet requirements for both push layer expansion and drug release. PPOP is suitable for poorly soluble drugs (Lin *et al*., 2022), though its preparation process is complex and demands precise control over excipient properties and dosage to ensure stable, consistent drug release (Nakajima *et al*., 2018).

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Sandwiched osmotic tablets (SOTS)

In this system, a push layer is positioned between two drug layers, with two delivery orifices (Fig. 4). In an aqueous environment, the intermediate push layer containing a swelling agent undergoes swelling, resulting in drug release through the orifices located on either side of the tablet (Qin *et al*., 2014). SOTS work well with drugs that cause local GI mucosal irritation (Gao *et al*., 2020). They can avoid drug layer identification technology and greatly reduce production costs (Kumaravelrajan *et al*., 2010).

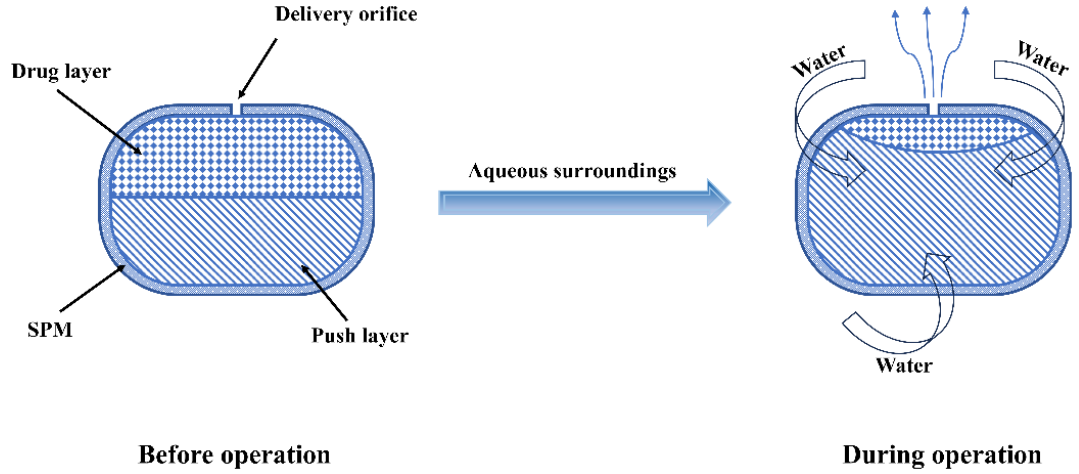

Fig. 3: Schematic diagram showing the drug release mechanism from a PPOP tablet actuated by the push layer through a single orifice.

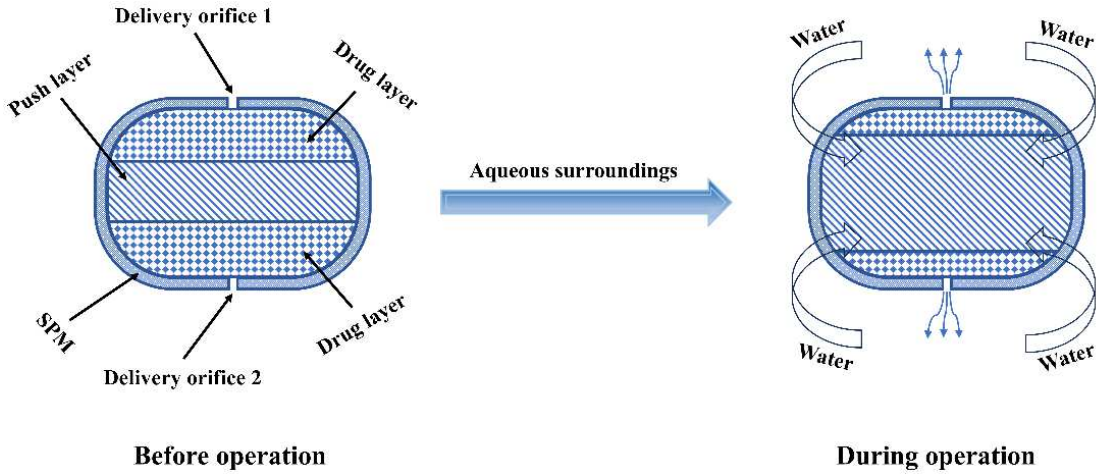

Fig. 4: Schematic diagram showing the drug release mechanism from SOTS, where different drugs are released through specific orifices actuated by the push layer.

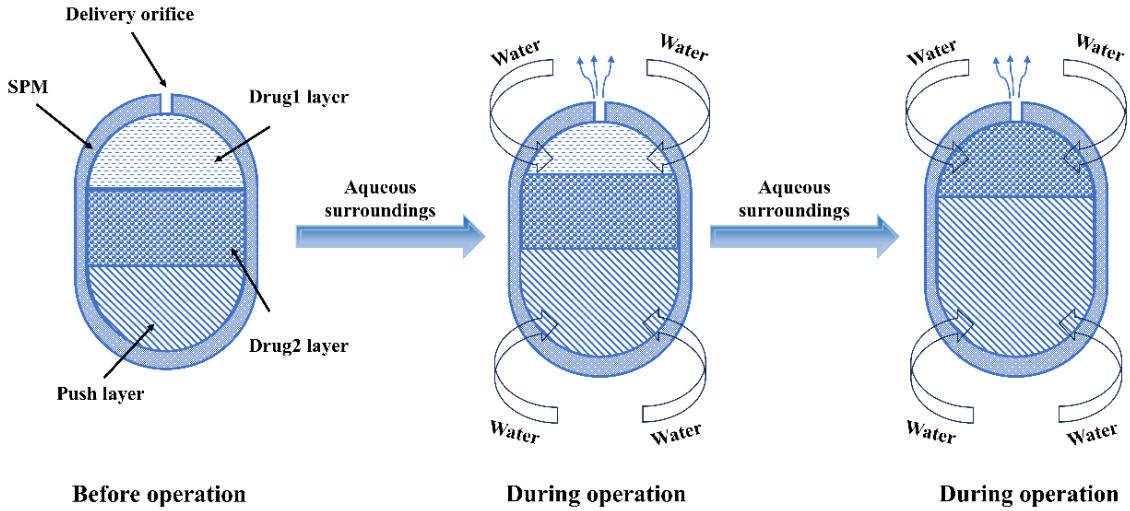

Fig. 5: Schematic diagram illustrating the sustained/controlled release mechanism of drugs located in distinct planes from a PSOP tablet, actuated by the push layer through a single orifice.

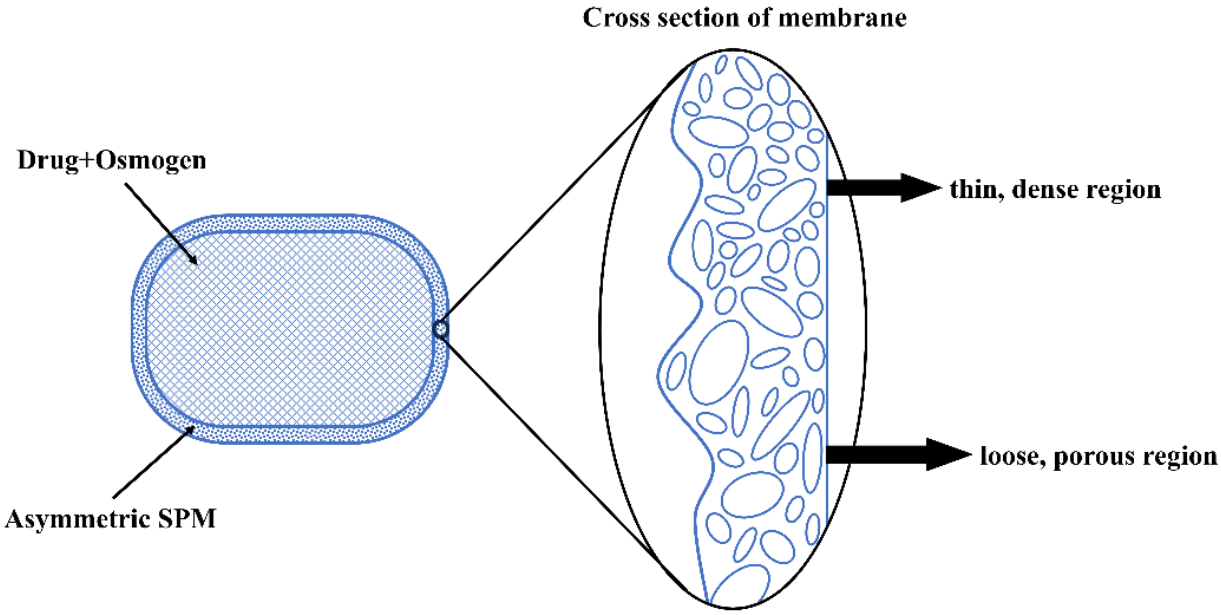

Fig. 6: Schematic diagram of the asymmetric membrane osmotic tablet and its asymmetric membrane cross-sectional structure.

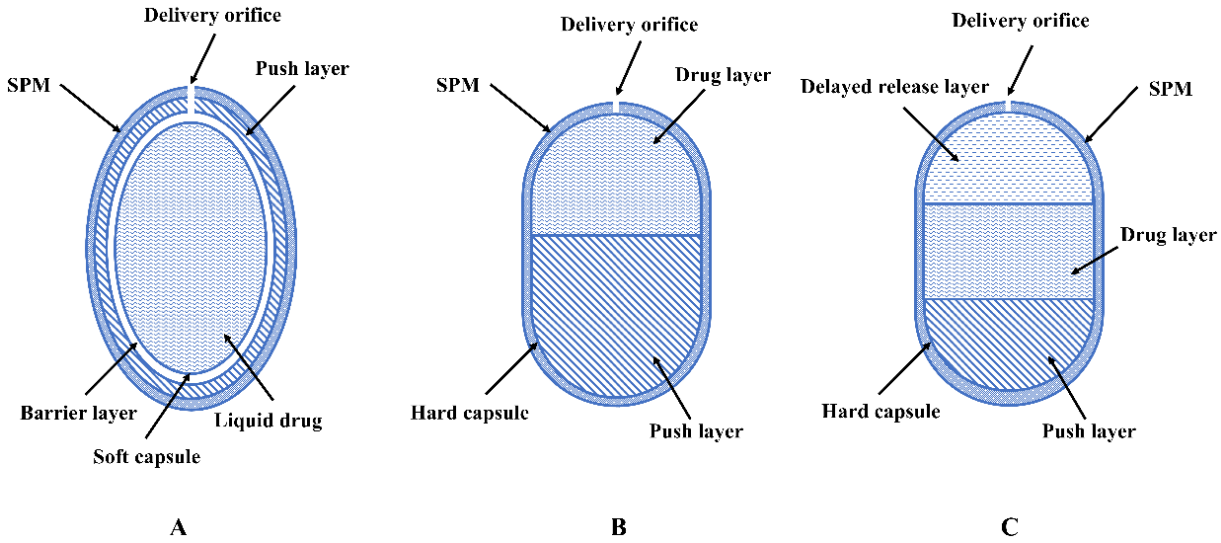

Fig. 7: Liquid osmotic pumps (A) Soft capsule, (B) Hard capsule and (C) Time-delay.

Push-stick osmotic pump (PSOP)

PSOP (Fig. 5) are suitable for drugs requiring prolonged, stable and precisely controlled release, particularly those used in chronic disease treatment (Malaterre *et al*., 2009). Their key advantage is that the piston's mechanism ensures consistent and complete drug release. However, this system's limitations include a complex structure (increasing manufacturing costs) and stringent durability requirements for materials/components.

Specific types

Monolithic osmotic system

The typical formulation comprises a homogeneous core containing the API and osmotic agents, surrounded by an SPM (Liu *et al*., 2000). The preparation ensures uniform mixing of components while maintaining tablet integrity and film coating continuity (Liu and Che, 2006). This system is suitable for drugs requiring stable, long-term release at moderate doses, particularly for chronic disease management. Its key advantage is the integrated structure, which simplifies the preparation while ensuring stable, consistent drug release (Zhao *et al*., 2016). However, it is not suitable for poorly soluble drugs or high-dose formulations, requiring rigorous material selection and process control (Li *et al*., 2012).

Colon-targeted oral osmotic system (CT-OROS)

CT-OROS is suitable for drugs requiring localized

therapeutic effects in the colon, such as those treating irritable bowel syndrome and colitis (Nie *et al*., 2020). The system may be a single osmotic agent or a hard gelatin capsule and push-pull system with 5 or 6 osmotic units. The system features an enteric coating that safeguards the drug-containing core from gastric juice and facilitates a consistent drug release rate in the colon. Modifications can enhance the bioavailability of poorly soluble drugs, such as through self-emulsification or complexation with cyclodextrins (Jin *et al*., 2018; Shao *et al*., 2020).

Buccal osmotic tablet

Buccal osmotic tablets deliver drugs directly to systemic circulation via the jugular vein through oral mucosa absorption (primarily buccal mucosa). They bypass hepatic first-pass effect, enabling rapid onset and enhanced bioavailability (Bakr *et al*., 2022). These formulations suit drugs susceptible to acid degradation, enzymatic breakdown in the GI tract, or hepatic first-pass inactivation. Alza has patented buccal osmotic tablets containing nicotine base, tendosynon and nystatin. Design considerations include: incorporating gel-forming agents (e.g., PEO or hydroxypropyl cellulose) into the drug layer to maintain structural integrity during oral activities and ensure consistent drug release; implementing patient-notification methods (e.g., flavoring agents in the push layer or transparent coatings) to signal drug depletion.

Asymmetric membrane osmotic tablet

The distinctive structure of the asymmetric SPM (Fig. 6) is key to its functionality. Membranes prepared with different excipients and processes exhibit significant variations in pore size and permeation properties (Patel *et al*., 2012). Asymmetric membrane osmotic tablets are ideal for drugs requiring precise regulation of release kinetics, especially those susceptible to GI degradation (Yang *et al*., 2016). This design offers fine-tuned release control, enhancing stability and efficacy (Guan *et al*., 2010).

Self-emulsified osmotic tablet (SEOT)

Self-emulsifying agents enhance drug bioavailability. The selection of surfactants and oil phases with self-emulsifying properties, such as polyoxyethylene castor oil and glycerol trioleate, ensures the formation and stability of the self-emulsifying layer (Yanfei *et al*., 2017). Upon entering the GI tract, SEOT spontaneously forms an emulsion through moisture-mediated action, facilitating drug dissolution. Osmotic action through the SPM then enables continuous drug delivery into the GI tract (Wei *et al*., 2007). SEOT is an effective delivery system for poorly soluble drugs or those requiring enhanced bioavailability, improving efficacy while reducing adverse effects (Huang *et al*., 2018).

Effervescent osmotic tablet

This system employs effervescent compounds that generate carbon dioxide upon contact with gastric fluid (Li *et al*., 2004). The resulting gas expansion propels drug suspensions, preventing orifice blockage. This mechanism is particularly advantageous for drugs with pH-dependent solubility that may precipitate in the stomach's acidic environment, causing gastric irritation. Sodium bicarbonate is a commonly used effervescent agent.

Floating osmotic pump

There are several methods for making floating osmotic tablets (FOT). A monolithic osmotic tablet system and an air pocket-a section of the capsule that is filled with air-were used to create an FOT that provided buoyancy (Zhang *et al*., 2009); developed a floating EOP tablet by adding a hydrophilic polymer to the core chamber, in which a gas generating agent produces gas which is then entrapped by hydration of the gel layer to create buoyancy (Khan *et al*., 2011); used stereolithography three-dimensional printing technology to fabricate a bandage-type buoyancy device in which the osmotic core is snap-fitted and buoyancy is generated by an external device (Ni *et al*., 2024).

Liquid oral osmotic system

Drugs in liquid form can be administered via an oral liquid osmotic pump. Soft capsule, hard capsule and time-delay liquid osmotic pumps (depicted in Fig. 7) are the three main varieties of liquid oral osmotic pumps (Malaterre *et al*., 2009; Patel and Parikh, 2017). Each of these consists of three distinct layers: a liquid medication layer, an osmotic driving layer and an SPM coating. Time-delay liquid osmotic pumps are appropriate for pulsed delivery of liquid medications, whereas soft capsule and hard capsule liquid osmotic pumps are more suitable for continuous drug delivery. However, liquid medications may present logistical challenges in storage and transportation, necessitating high packaging material tightness and stability.

Comparative analysis of oral osmotic pump systems

Collectively, these specialized osmotic systems address unique therapeutic challenges-such as site-specific delivery, bioavailability enhancement and liquid API compatibility-complementing conventional single- and multichamber designs (see comparative analysis in Table 2).

Clinical translation and commercial viability of oral osmotic pumps

The clinical translation potential of oral osmotic pump systems, as evaluated in table 3, hinges on a synergistic alignment between the drug's physicochemical properties, therapeutic needs and scalable manufacturing feasibility. This theoretical framework is robustly validated by their proven commercial success, with numerous marketed products spanning a wide spectrum of BCS classifications and employing diverse designs from elementary to push-pull osmotic pumps, demonstrating the practical utility of this technology in addressing key clinical challenges such as delivering poorly soluble drugs and enabling precise, sustained release (Table 4).

Table 2: Comparative analysis of oral osmotic pump systems

System type	Subtype/Example	Key advantages	Major limitations
Single-chamber systems *(Single drug compartment)*	EOP (Elementary osmotic pump)	Simple design. Sustained zero-order release. pH/physiology-independent release. Ease of scale-up.	Limited to soluble drugs. Incomplete release for poorly soluble drugs. Requires laser drilling.
	CPOP (Controlled-porosity osmotic pump)	No laser drilling needed. Tunable release via pore-formers. Lower burst release risk.	Sensitive to pore-former type/dose. Complex optimization of release rate. Membrane integrity critical.
	SCOP (Single composition osmotic pump)	No push layer required. Simplified manufacturing. Cost-effective. Consistent release.	Unsuitable for poorly soluble/high-dose drugs. Narrow therapeutic dose range.
Multichamber systems *(Multi-compartment synergy)*	PPOP (Push-pull osmotic pump)	Effective for poorly soluble drugs. Precise zero-order release. High-dose capability.	Complex design (bilayer compression). Tight control of excipient properties/dosing required. High cost.
	SOTS (Sandwiched osmotic tablets)	Dual-side release reduces mucosal irritation. Avoids layer identification technology. Lower cost than PPOP.	Custom equipment needed. Swelling behavior of middle layer requires optimization.
	PSOP (Push-stick osmotic pump)	Piston ensures complete drug expulsion. Exceptional release consistency.	Complex assembly. High material durability requirements. Very high cost.
Specific types *(Specialized designs)*	Monolithic osmotic system	Homogeneous core simplifies manufacturing. Stable long-term release.	Poor compatibility with insoluble/high-dose drugs. Rigorous material selection needed.
	CT-OROS (Colon-targeted oral osmotic system)	Enteric coating resists gastric acid. Site-specific colonic delivery. Enhanced local efficacy.	Complex design (multi-unit/multilayer). High cost.
	SEOT (Self-emulsifying osmotic tablets)	Self-emulsification boosts bioavailability. Reduces dose/frequency for BCS II/IV drugs.	Stability challenges in emulsion system. Excipient compatibility issues.
	FOT (Floating osmotic pump tablet)	Gastric retention prolongs duration of action. Improves local drug concentration.	Buoyancy control variability. High inter-subject GI retention differences.
	Asymmetric membrane osmotic tablets	Tailored membrane controls release kinetics. Protects GI-labile drugs.	Complex manufacturing (membrane fabrication). Batch-to-batch consistency challenges.

The existence of these commercial products not only underscores the maturity and reliability of osmotic pump platforms but also provides a concrete reference for formulators in selecting and optimizing the most appropriate system for future drug development.

DISCUSSION

Oral osmotic pump release factors

Drug

Drug selection

The choice of an appropriate drug is crucial for osmotic

drug delivery systems, significantly influencing performance. Osmotic tablets are commonly used for drugs with short biological half-lives (typically 2-6 hours) (Zhang *et al*., 2011), though half-life is not the primary selection criterion (Ogueri and Shamblin, 2022). The Biopharmaceutical Classification System (BCS), developed by Corrigan and Amidon, divides drugs into four main groups: Class I drugs are defined by their high permeability and high aqueous solubility, resulting in high absorption rate. Class II drugs have low solubility but high permeability. Supersaturated solutions may be used to enhance bioavailability for these drugs. Class III and IV drugs both exhibit low permeability, though Class III shows high solubility while Class IV has low solubility leading to poor bioavailability (Flanagan, 2019). In sustained-release development, BCS classification provides a framework for selecting drug delivery strategies. Classes I and II drugs are preferred for sustained-release formulations due to their permeability and lack of absorption windows.

Drug solubility adjustment method

A drug with excessive solubility will result in rapid dissolution, which in turn affects the zero-order release profile. To address this, several adjustment methods can be employed (Cheng *et al*., 2018; Marbach *et al*., 2017; Wang *et al*., 2021), including:

1. Alteration of the salt type;
2. Incorporation of a release modifier;
3. Utilization of ion-specific effects.

The solubility of drugs can be adjusted by a number of methods (Yu *et al*., 2021; Zhang *et al*., 2020; Shokri *et al*., 2008), including:

1. The addition of β-cyclodextrin;
2. The application of solid dispersion technology;
3. The formation of salts;
4. The addition of acid and alkaline substances;
5. The control of crystal shape.

Osmotic pressure

Osmotic polymers are the primary excipients that generate osmotic pressure. They are typically highly hydrophilic and swellable, capable of rapidly absorbing and swelling upon contact with water, thereby creating a significant osmotic pressure difference across the formulation (Shokri *et al*., 2008). This pressure differential is the main factor causing the drug release. Ideal osmotic polymers must exhibit sufficient water-absorbent and swelling properties to generate the requisite osmotic pressure for drug release while demonstrating biocompatibility and stability to ensure safety and efficacy in the GI environment (Kan *et al*., 2015; Li *et al*., 2008). The molecular weight (MW) of the polymer is a critical physical characteristic that governs its swelling kinetics and gel strength. For instance, studies employing PEO have demonstrated that its functionality within osmotic pumps is highly dependent on MW, with available grades ranging from 100 to 5000 kDa. Lower MW PEO (e.g., 200 kDa) facilitates rapid hydration and formation of a less viscous gel, favoring expulsion from the drug layer, whereas higher MW PEO (e.g., 5000 kDa) provides a larger sustained swelling force, ideal for the push layer in systems like PPOP (Nakajima *et al*., 2018; Brighenti and Cosma, 2020). The concentration of osmogenic polymers directly influences osmotic pressure magnitude, subsequently affecting drug release rate. Generally, increased polymer concentration increases osmotic pressure, accelerating drug release. Additionally, the polymers' chemical and physical characteristics govern drug release kinetics (Gupta *et al*., 2015). Therefore, the selection of polymer type, molecular weight and concentration must be tailored to the specific drug and desired release profile. Common osmogenic polymers include PEO, high molecular weight PEG and polyhydroxymethacrylate.

Semi-permeable membrane

SPM material

The permeability coefficient (K) of an SPM to water is an important parameter that reflects the properties of the membrane. The most commonly utilised SPM materials are cellulose acetate and ethyl cellulose, which exhibit excellent film-forming properties, mechanical strength and water permeability. They also effectively control drug release rates (Aziz *et al*., 2024). Plasticisers are frequently incorporated to improve membrane mechanical properties, enabling them to withstand osmotic pressure in the core. Common plasticisers include phthalates, PEG400 and glycerol esters (Guan *et al*., 2010; Li *et al*., 2018).

Thickness of SPM

The rate of zero-order release of osmotically pumped controlled release tablets is inversely proportional to membrane thickness (Yuan *et al*., 2019). An increase in film thickness prolongs water permeation time through the film and decreases the drug release rate. Conversely, a decrease in film thickness increases the drug release rate (Pravinkumar *et al*., 2024). However, an excessively thin SPM may compromise controlled release due to the deterioration of mechanical properties or the risk of membrane rupture. For example,It is reported that the coating weight of the cellulose acetate membrane was reported to be 8.6 ± 0.8 mg for an EOP and 23.6 ± 1.2 mg for a larger PPOP tablet (Nakajima *et al*., 2018). Considering a uniform coating density and tablet surface area, these coating weights correspond to membrane thicknesses typically falling within the range of several tens to a few hundred micrometers. Achieving a thickness within this range is therefore critical to balance robust mechanical integrity against internal osmotic pressure with adequate water permeability.

Table 3: Clinical translation potential of oral osmotic pump systems

System type	Subtype/ Example	Ideal drug profile	Manufacturing complexity	Clinical translation potential	Key rationale
Single-chamber systems	EOP	BCS Class I/III drugs (high solubility)	Low	High	A mature, robust platform for BCS I/III drugs. Simple design facilitates low-cost, large-scale production and ensures high reliability.
	CPOP	Low-moderate solubility drugs (with solubilizers)	Moderate	High	High versatility and adaptability for drugs with varying solubility. The absence of laser drilling reduces manufacturing barriers and cost.
	SCOP	Moderate-solubility drugs (BCS Class I)	Low-Moderate	Moderate	A cost-effective solution for moderate-solubility drugs, ideal for cost-sensitive chronic therapies, albeit with a narrower scope.
Multichamber systems	PPOP	BCS Class II/IV drugs (low solubility)	High	Very High	The gold-standard for delivering poorly soluble drugs (BCS II/IV), a major therapeutic class. Proven by multiple marketed products.
	SOTS	Irritant/Combination drugs	Moderate-High	Moderate	Valuable for reducing GI irritation or delivering combinations, but reliance on specialized equipment may hinder widespread adoption.
	PSOP	Chronic therapies	Very High	Low	Offers unparalleled release consistency for critical therapies, but extreme manufacturing complexity and cost are significant barriers.
Specific types	CT -OROS	Colonic disease drugs (e.g., mesalazine)	High	High	Addresses an unmet need for targeted colonic delivery, offering a superior therapeutic option for inflammatory bowel disease.
	SEOT	Poorly soluble drugs (BCS II/IV)	High	High	A highly innovative strategy to overcome the pervasive challenge of poor bioavailability, holding great promise for BCS II/IV drugs.
	FOT	Gastric-acting/Alkaline drugs	Moderate-High	Moderate	Useful for gastric retention, but variable buoyancy control and GI physiology can lead to inconsistent *in vivo* performance.
	Asymmetric membrane osmotic tablets	Degradation-prone APIs (e.g., peptides)	High	Moderate	Provides superior release control for sensitive APIs, but complex membrane fabrication poses challenges for consistent mass production.
	Liquid oral osmotic system	Liquid APIs/Extreme insolubility cases	High	Moderate	Enables delivery of liquid formulations, but stability and leakage risks require sophisticated and costly packaging solutions.

Drug release orifices

Drug release orifices can be created through mechanical drilling, laser drilling, in situ channel systems, or by incorporating pore-forming agents in the SPM (Almoshari, 2022; Yuan *et al*., 2019). The choice of technology dictates the achievable orifice size and precision. Laser drilling is widely utilized due to high precision and operational simplicity (Gundu *et al*., 2021), enabling the creation of orifices as small as 0.5-1.5 μm, which are typical for EOP (Missaghi *et al*., 2013). By modulating laser power, pulse frequency and irradiation time, precise orifices with regular shapes can be created at designated locations (Shakur Sheaikh, 2022).

Table 4: A number of marketed oral osmotic products

Brand name	Active pharmaceutical ingredients	BCS Class	Design
Efidac 24	Pseudoephiderine	I	EOP
Efidac 24	Chlorpheniramine meleate	I	EOP
Altoprev	Lovastatin	II	EOP
Calan SR	Verapamil	IV	EOP
Minipress XL	Prazosin	III	EOP
Sudafed 24	Pseudoephedrine	I	EOP
Volmax	Albuterol	III	EOP
Flexeril XL	Cyclobenzaprine	I	EOP
Elafax XR	Venlafaxine HCl	I	EOP
Alpress LP	Prazosin	III	PPOP
Cardura XL	Oxybutinin chloride	I	PPOP
Dynacirc CR	Isradipine	II	PPOP
Glucotrol XL	Glipizide	II	PPOP
Covera HS	Verapamil	IV	PPOP
Ditropan XL	Oxybutynin chloride	I	PPOP
Invega	Paliperidone	II	PPOP
Procardia XL	Nifedipine	II	PPOP
Exalgo/Jurnista	Hydromorphone	II	PPOP
Cardura CR	Doxazosin mesylate	I	PPOP
Oxycontin	Oxycodone	IV	PPOP
Concerta	Methylphenidate HCl	II	PSOP
Topamax	Topiramate	III	PSOP
Acu System C	Vitamin C	III	CPOP
Teczem	Enalapril/diltiazem	III/I	CPOP
Tiamate, Dilacor XR	Diltiazem HCl	I	CPOP
Tegretol XL	Carbamazepine	II	SEOP
Actoplus METXR	Pioglitazone HCl/Metformin HCl	II/III	SCOP
Fortamet	Metformin HCl	III	SCOP

For systems that rely on the extrusion of a gel-forming core, such as push-pull osmotic pumps, larger orifices are required; studies employing mechanical drilling have utilized diameters ranging from 0.6 to 1.6 mm for this purpose (Patel *et al*., 2012). The dimensions of these orifices significantly influence drug release rates. Excessively large orifices can lead to non-constant release rates and burst release (Li *et al*., 2008; King *et al*., 2022; Ogueri and Shamblin, 2022), whereas smaller orifices may reduce efficacy by increasing flow resistance. Given these considerations, the optimal orifice size and number are system-specific and must be empirically determined to match the viscosity of the hydrating formulation and the targeted release rate, thereby ensuring consistent performance without orifice blockage or premature membrane failure.

CONCLUSION

Osmotic-driven drug delivery systems, particularly oral osmotic-driven systems (OODS), represent significant advancements in drug delivery. These systems utilize osmotic pressure to maintain stable drug release control, largely unaffected by pH and physiological variations. This guarantees reliable and predictable therapeutic outcomes with excellent *in-vitro in-vivo* correlation. OODS exhibits broad applicability across drugs with diverse physicochemical profiles. However, the advancement of these systems is constrained by several challenges, including drug/formulation limitations, interpatient variability, manufacturing complexities, idealized mechanistic models and insufficient excipient exploration.

Looking forward, overcoming these challenges and unlocking the full potential of next-generation osmotic pumps will rely on the integration of three key technological frontiers:

Computational Modeling and AI: The integration of AI and computational modeling can significantly enhance development efficiency and clinical translation potential. For instance, the optimization of critical formulation

parameters using artificial neural networks and response surface methodology, coupled with physiologically based pharmacokinetic (PBPK) simulations, can accurately predict *in-vivo* behavior (Saleem *et al*., 2025). This approach can address the limitations of idealized mechanistic models and guide personalized design to mitigate interpatient variability.

Advanced Manufacturing Technologies: Innovative fabrication strategies, such as semi-solid extrusion 3D printing, can overcome the limitations inherent in conventional coating and laser-drilling processes. This technology enables the integral fabrication of core-shell osmotic pump tablets, establishing a novel manufacturing paradigm for developing structurally sophisticated systems with precisely regulated release profiles (Chen *et al*., 2024). This can directly address the manufacturing complexity and cost barriers associated with traditional methods.

Smart Material Science: The exploration and application of novel materials are crucial. Leveraging functionalized materials, such as magnetic nanoparticles for energy-efficient osmotic agent regeneration (Navarro-Tumar *et al*., 2024), can pioneer novel avenues for smart osmotic pump drug delivery systems. Continued efforts in material innovation will be vital to address drug stability issues, enhance biocompatibility and create more responsive and adaptive systems.

In conclusion, while oral osmotic pumps are a mature technology, their evolution is far from complete. By addressing existing challenges through the strategic adoption of computational intelligence, advanced manufacturing and smart materials, the next generation of OODS can achieve unprecedented levels of precision, efficacy and personalization in drug delivery.

Acknowledgements
Not applicable

Authors' contributions
Xintao Qiu: Investigation and writing; Jing Shu: Investigation; Yuanyuan Chen: Investigation; Qing Min and Yuting Bai: Review and editing; supervision; Shuanglin Qin and Hui Yao: Review and editing; supervision; funding acquisition, conceptualization. All images are drawn by Xintao Qiu. All authors approved the final manuscript.

Funding
This work was supported by the Research Project of Hubei Provincial Department of Education (B2023166).

Data availability statement
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
Not applicable

Conflict of interest
The authors have no relevant financial or non-financial interests to disclose.

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