Osmotic Drug Delivary System: Smart Solution for Sustained Targeted Therapy

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Abstract— **Osmotic drug delivery systems (ODDS) represent one of the most reliable and predictable controlled-release platforms, offering sustained and targeted drug delivery independent of gastrointestinal variables. These systems operate on osmotic pressure–driven mechanisms that ensure zero-order release, improved pharmacokinetic stability, and reduced dosing frequency Recent advancements, including nano-engineered membranes, asymmetric coating technologies, and colloidal osmotic cores, have significantly expanded ODDS applicability for poorly soluble and stability-sensitive drugs Push–Pull Osmotic Pumps (PPOP), Controlled-Porosity Osmotic Pumps (CPOP), SEOP, and enteric osmotic capsules provide versatile designs for extending release up to 24 hours while maintaining reproducibility and minimal dose dumping Additionally, innovations such as pH-responsive membranes for colon targeting and AI-based formulation optimization demonstrate the emergence of smart, next-generation osmotic systems Despite their advantages, limitations such as membrane sensitivity, manufacturing complexity, and solubility challenges still persist This review consolidates the principles, mechanisms, types, formulation strategies, recent advancements, applications, advantages, and limitations of ODDS based on research, highlighting their growing potential as a smart solution for sustained and targeted therapy.**

Keywords - Osmotic drug delivery system; sustained release; push–pull osmotic pump; controlled porosity; asymmetric membrane; targeted delivery; zero-order release; nanomembrane; AI optimization.

I. INTRODUCTION

Controlled drug delivery systems are designed to maintain steady plasma concentrations and reduce dosing frequency, thereby improving patient adherence and therapeutic outcomes (Shivam Gavandare et al., 2020).Among these systems, osmotic drug delivery systems (ODDS) are regarded as one of the most reliable approaches, as they use osmotic pressure as the primary driving force for drug release, enabling reproducible and predictable kinetics (Khan et al., 2022).ODDS offer a major advantage by being largely independent of gastrointestinal factors such as pH, motility, and food intake, which often affect conventional sustained-release formulations (Singh et al., 2023). The fundamental mechanism is based on the movement of water across a semipermeable membrane into a core containing the drug and osmogenes, generating osmotic pressure that pushes the drug solution or suspension through a delivery orifice (Azhar et al., 2021).Over the years, several osmotic designs have been developed, including the Elementary Osmotic Pump (EOP), Push–Pull Osmotic Pump (PPOP), and Controlled-Porosity Osmotic Pump (CPOP), each tailored for drugs with different solubility profiles (Patel et al., 2024). Clinical success of osmotic systems is supported by multiple marketed products, such as osmotic formulations of nifedipine, glipizide, paliperidone, and hydromorphone, which deliver sustained therapeutic action with reduced plasma fluctuations (patel et al., 2024).Modified systems such

as PPOP and osmotic capsules have expanded ODDS utility to poorly water-soluble drugs and targeted GI delivery, addressing limitations of earlier systems (Ymer Yet al., 2023) Recent advancements highlight the potential of next-generation osmotic devices, incorporating nanotechnology, smart polymeric membranes, micro-osmotic pumps, and intelligent controlled release mechanisms (Shao et al., 2020)Due to their high reliability and predictable release profile, ODDS are particularly suitable for chronic diseases like hypertension, diabetes, ADHD, schizophrenia, and chronic pain, where stable drug exposure is essential (Khan et al., 2022)Overall, osmotic drug delivery systems represent a robust, evolving, and intelligent platform for sustained and targeted therapy, offering distinct advantages over many traditional controlled release technologies (Patel et al., 2024)

II. HISTORICAL BACKGROUND

The concept of osmotic drug delivery originated from the basic principles of osmosis, where solvent movement across a semipermeable membrane generates a controllable pressure gradient suitable for sustained drug release (Shivam-Gavandare et al., 2020).

The earliest approach was inspired by Rose and Nelson's implantable osmotic pump (1955), which demonstrated the feasibility of using osmotic pressure for continuous drug infusion (Khan et al., 2022). Higuchi and Leeper later introduced the first oral osmotic pump design, known as the Elementary Osmotic Pump (EOP), establishing the foundation for oral osmotic drug delivery technologies (Patel et al., 2024)

EOP became a milestone because it enabled zero-order release for water-soluble drugs, marking a significant advancement over conventional matrix diffusion systems (Singh et al., 2023). To address poorly water-soluble drugs, the Push–Pull Osmotic Pump (PPOP) was introduced, incorporating a bilayer core with a push layer and drug layer that improved the release mechanism for low-solubility molecules (Kumar et al., 2023). Further developments led to the Controlled Porosity Osmotic Pump (CPOP), where pore-forming agents in the coating created in-situ pores, eliminating the need for a laser-drilled orifice (Azhar et al., 2021).

During the 1980s–2000s, several osmotic pump–based marketed products were introduced, including nifedipine GITS, glipizide GITS, and paliperidone OROS®, validating the technology in clinical use (Shivam-Gavandare et al., 2020).

With advancements in excipients and polymer science, newer systems incorporated improved semipermeable membranes, high-efficiency osmogens, and push-layer polymers that enhanced stability and release control (Patel et al., 2024)

Recent research focuses on integrating nanotechnology, microfabrication, and smart polymers into osmotic devices, marking the beginning of next-generation intelligent osmotic platforms (Shao et al., 2020) Today, osmotic systems represent a mature yet continually evolving drug delivery strategy, widely recognized for their precision, reproducibility, and suitability for chronic therapies (Khan et al., 2022)

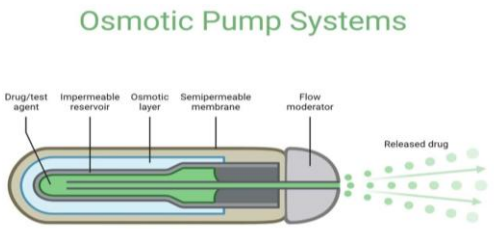
III. PRINCIPLE

Osmotic drug delivery systems operate on the basic principle of osmosis, where water naturally moves from a region of lower solute concentration to higher solute concentration across a semipermeable membrane (Shivam-Gavandare et al., 2020).

The osmotic pressure generated inside the system becomes the driving force for drug release, enabling controlled and consistent output independent of external physiological conditions (Khan et al., 2022). A semipermeable membrane allows water to enter but restricts the movement of drug and excipients, ensuring unidirectional flow and maintaining release precision (Singh et al., 2023).

Osmotic systems follow near zero-order release kinetics, meaning the drug is released at a uniform rate over an extended period (Patel et al., 2024). The magnitude of osmotic pressure is governed by osmogens (e.g., salts, sugars), which absorb water and swell or dissolve to push the drug out (Azhar et al., 2021).

IV. MECHANISM OF ACTION (MOA)



Upon administration, gastrointestinal fluids permeate through the semipermeable membrane because of the osmotic gradient between the external medium and the core (Shivam-Gavandare et al., 2020).

Water influx dissolves or suspends the drug inside the core, forming a saturated drug solution or gel inside the tablet (Patel et al., 2024).

As more water enters, osmotic pressure builds up within the system, producing a controlled, constant internal hydrostatic force (Khan et al., 2022).

This pressure pushes the drug solution out through a laser-drilled orifice or in-situ generated pores, depending on the device type (Singh et al., 2023).

In push–pull systems (PPOP), the push layer swells significantly when hydrated, generating mechanical pressure to expel the drug from the drug layer, especially for poorly soluble drugs (Kumar et al., 2023).

Controlled-porosity osmotic pumps (CPOP) allow drug release through micropores formed in the membrane, eliminating the need for orifice drilling (Azhar et al., 2021).

Because the driving force (osmotic pressure) remains constant, the drug release rate becomes independent of gastric variables like pH, food, agitation, or motility (Shao et al., 2020). Drug release continues until the entire core is depleted, after which the exhausted shell is excreted intact (Khan et al., 2022)

V. TYPES OF OSMOTIC DRUG DELIVERY SYSTEMS

1. Elementary Osmotic Pump (EOP)

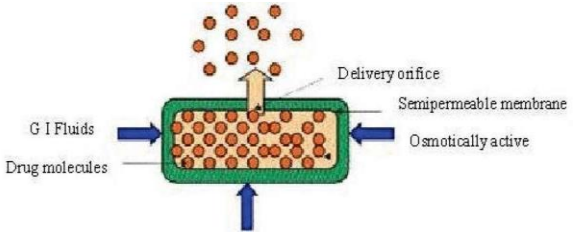


Fig No.2.Elementary Osmotic Pump

EOP is the earliest and simplest osmotic system consisting of a drug core surrounded by a semipermeable membrane with a laser-drilled orifice. It provides zero-order release for watersoluble drugs (Patel et al., 2024). It delivers drug solution at a constant rate until the core is exhausted (Singh et al.2022)

1. Push-Pull osmotic pump (PPOP)

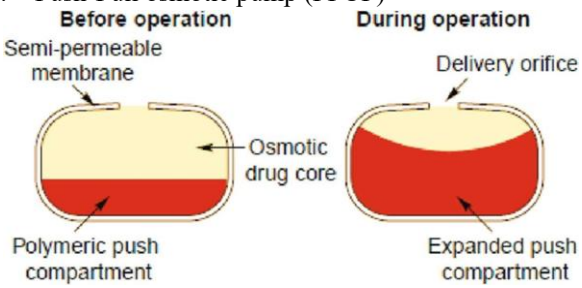


Fig.no Push pull osmatic pump

PPOP is a bilayer tablet containing a drug layer and a swelling push layer.

The push layer expands upon hydration, forcing the drug out through the delivery orifice, making the system ideal for poorly water-soluble drugs (Kumar et al., 2023).

It is widely used in marketed systems like Procardia XL® and Glucotrol XL® (ShivamGavandare et al., 2020).

3. Controlled-Porosity Osmotic Pump (CPOP)

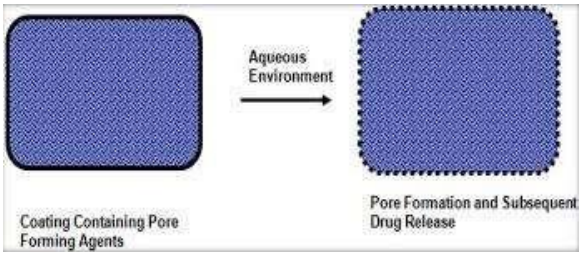


Fig No.4.Controlled-Porosity Osmotic Pump

CPOP uses pore-forming agents such as PEG or sorbitol in the membrane.

When exposed to water, these agents dissolve, generating micropores for drug release without the need for laser drilling (Azhar et al., 2021). This simplifies manufacturing and avoids orifice blockage (Khan et al., 2022).

4. Multi-Particulate Osmotic Systems (MOPS)

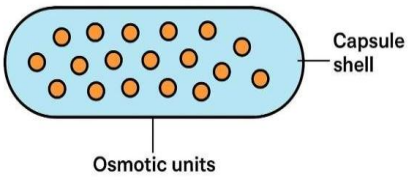


Fig no.5.multi-particulate osmotic system

These systems contain small osmotic units (mini-tablets or pellets) inside a capsule.

They offer reduced risk of dose dumping, uniform GI distribution, and more reproducible absorption (Shao et al., 2020).

5. Osmotic Capsule Delivery Systems (Osmotic)

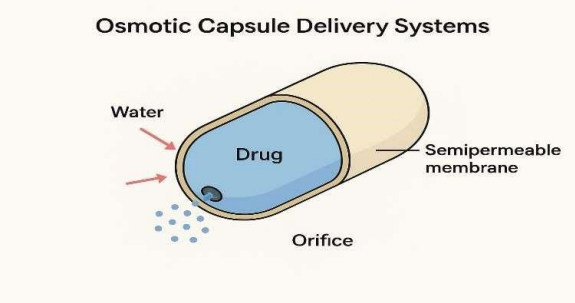


Fig no.6.Osmotic capsule delivery system

These are capsule-based osmotic platforms where the shell acts as a semipermeable membrane. Used for controlled release of drugs like metformin and site-specific delivery to the intestine or colon (Li, X & Chen, Y et al., 2020).

6. Sandwiched Osmotic Tablets (SOTS)

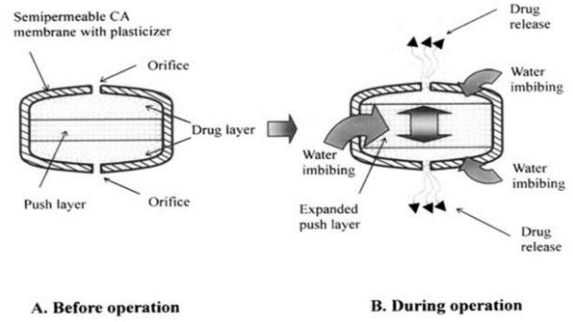
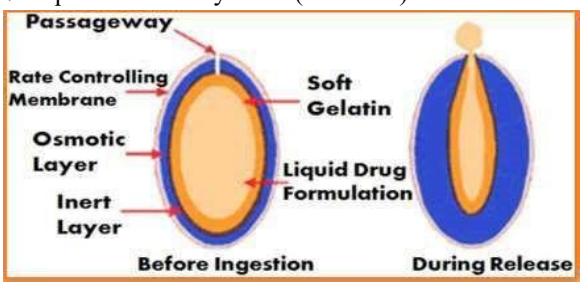


Fig No.7.Sandwhich Osmotic Tablets

SOTS consist of a drug layer sandwiched between two push layers. Hydration causes both layers to swell and push the drug out in a symmetric, controlled fashion. Useful for pulsatile or modulated release (Patel et al., 2024)

7.Liquid Osmotic Systems (L-OROS)



These systems deliver liquid formulations using osmotic pressure.

They use a liquid drug compartment and an osmotic agent compartment separated by a movable partition. Common for poorly compressible or unstable solid drugs. (Shivam-Gavandare et al., 2020)

8. Asymmetric Membrane Osmotic Tablet (AMOT)

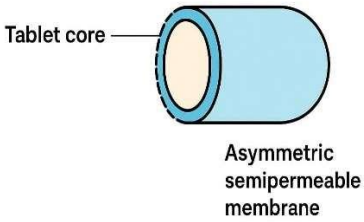


Fig.no.9. Asymmetric Membrane osmotic tablet

AMOTs use an asymmetric semipermeable membrane produced by phase inversion. This membrane allows high water permeability and controlled drug delivery without needing drilled orifices (Shao et al., 2020).

9. Telescopic Osmotic Systems

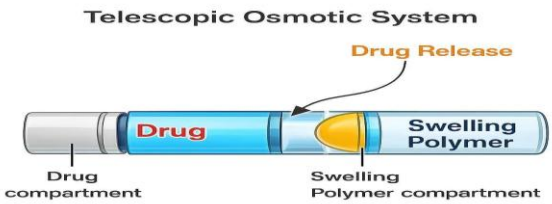


Fig.no.10. Telescopic osmotic system

Contain two compartments fitted together like a telescope—one with drug, one with swelling polymer. Ideal for high-potency and unstable drugs (Khan et al., 2022).

10. Micro-Osmotic Pumps

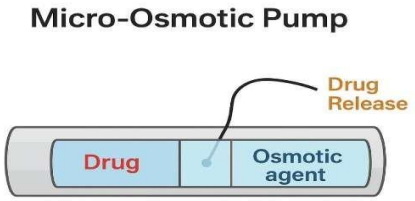


Fig.no.11. Micro-osmotic pump

Miniaturized devices used for implantable or precision delivery applications.

They are used in research, oncology, and long-term infusion therapies (Reed Berlet et al., 2025)

VI. COMPONENTS

1. Drug Core (Active Pharmaceutical Ingredient – API)

The central compartment contains the drug in dissolved or dispersed form.

Its solubility, particle size, and stability strongly influence osmotic release performance (Patel et al., 2024; Singh et al., 2023).

2. Osmotic Agents (Osmogens)

Osmogens such as sodium chloride, potassium chloride, mannitol, lactose, sorbitol, etc., create the osmotic pressure responsible for water influx. Higherosmogen concentration = higher release rate (Kumar, N., et al., 2023).

3. Semipermeable Membrane (SPM)

Made of polymers such as cellulose acetate, cellulose diacetate, ethyl cellulose, this membrane allows water entry but prevents drug and excipient movement .Its thickness and permeability determine the drug release rate (Shivam-Gavandare et al., 2020; Azhar et al., 2021).

4. Wicking or Hydrophilic Agents

These include povidone, PEG, sodium starch glycolate, crospovidone, which promote water uptake and distribute incoming water uniformly throughout the core (Khan et al., 2022).

5. Push Layer (for Push–Pull Osmotic Pump)

PPOP contains polymers like Carbopol, polyethylene oxide, hydroxypropyl methylcellulose (HPMC) that swell upon hydration and generate mechanical force to expel the drug—essential for poorly soluble drugs (Kumar, N., et al., 2023; Shao et al., 2020).

6. Pore Formers (for Controlled Porosity Systems)

Agents such as sorbitol, PEG 400, urea dissolve after contact with water and form micropores through which drug solution is released. Used specifically in CPOP systems to eliminate the need for laser drilling (Singh et al., 2023; Azhar et al., 2021).

7. Coating Plasticizers

Common plasticizers include diethyl phthalate, triacetin, PEG 400, which enhance flexibility, mechanical strength, and permeability of the membrane (Patel et al., 2024).

8. Delivery Orifice (Laser-Drilled Hole)

A precision orifice (~0.4–0.8 mm) is drilled using a CO_2 laser in EOP and PPOP systems. This acts as an outlet for the drug under osmotic pressure (Shivam-Gavandare et al., 2020).

9. Tablet Excipients (Binders, Fillers, Lubricants)

Binders (PVP, HPMC), fillers (lactose, MCC), and lubricants (magnesium stearate) help maintain tablet hardness, compressibility, and stability (Khan et al., 2022).

10. Capsule Shell (for Osmotic Capsules)

In capsule-based systems, the shell itself works as a semipermeable membrane, enabling controlled release from liquid or solid-filled osmotic capsules (Li, X., & Chen, y.et al., 2022)

VII. FORMULATION AND DEVELOPMENT STRATEGIES

1. Defining the Release Profile Requirement

Formulation begins with identifying whether zero-order, extended, delayed, or targeted GI release is needed. Osmotic systems are especially chosen when constant plasma levels are required for chronic therapy (Shivam-Gavandare et al., 2020).

2. Drug Solubility Assessment

Highly soluble drugs are suitable for EOP, whereas poorly soluble drugs require solubility enhancement

or conversion to a suspension-type PPOP system (Kumar, N., et al.,2023). Techniques used include: solid dispersion, cyclodextrin complexation, surfactants, or osmogen-supported solubilization (Azhar et al., 2021).

3. Selection of Osmogens
Common osmogens include NaCl, KCl, mannitol, fructose, lactose, sorbitol.
Their concentration directly affects water influx and release rate; hence optimization is essential (Patel et al., 2024; Khan et al., 2022).

4. Designing Drug Layer Composition
The drug layer typically includes the API, fillers (MCC, lactose), wicking agents (crospovidone), and solubilizers (PEG, PVP). For low-solubility drugs, suspension-type drug layers are used (Kumar, N., et al., 2023).

5. Designing Push Layer (for PPOP)
Push layer polymers like PEO, HPMC, Carbopol swell significantly on hydration and generate mechanical pressure to expel drug through the orifice (Shivam-Gavandare et al., 2020). The swelling capacity and viscosity grade of PEO directly control release (Shao et al., 2020).

6. Semipermeable Membrane Optimization

The membrane is usually made from cellulose acetate with plasticizers (PEG 400, triacetin). Thickness determines the rate of water entry and thus drug release (Patel et al., 2024).
CPOP systems include pore formers such as sorbitol or urea (Singh et al., 2023).

7. Laser Drilling of Orifice
A controlled orifice (~0.4–0.8 mm) is drilled using a CO_2 laser to ensure predictable release. Orifice diameter influences release rate and prevents dose dumping (Shivam-Gavandare et al., 2020).

8. In-Situ Pore Generation Strategy (CPOP)
Instead of drilling, pore-forming agents dissolve after contact with water, generating micropores that control release (Azhar et al., 2021).

9. Incorporation of Wicking Agents
Wicking materials like PVP, SSG, CCS, crospovidone are added to enhance water influx and uniform hydration of the core (Khan & Bhat et al., 2022)

10. Bilayer Compression Technology
Push–pull tablets are manufactured via bilayer compression, ensuring uniform layer thickness and consistent release behavior (Kumar, N., et al., 2023).

11. Asymmetric Membrane Technology (AMT)
Asymmetric membrane tablets are prepared by phase inversion method, producing a microporous outer layer that controls diffusion without drilling (Shao et al., 2020).

12. Use of Swellable Polymers in SEOP Devices
Swellable Elementary Osmotic Pumps (SEOP) utilize super-swelling polymers to generate internal pressure and modulate release, particularly for drugs requiring high push force (Shokri J., et al., 2020).

13. Polymer–Plasticizer Ratio Optimization
Membrane permeability depends on the polymer: plasticizer ratio, optimized using factorial design or Box–Behnken design (Shivam-Gavandare et al., 2020).

14. Use of Quality-by-Design (QbD)
Multiple studies (including on QbD of push–pull osmotic pump) used DoE, RSM, ANOVA to identify critical material attributes (CMAs) and critical process parameters (CPPs) (Khan & Bhat et al., 2022).

15. Film Coating Parameters
Critical variables include: spray rate, inlet temperature, pan speed, and coating weight gain — all affecting membrane uniformity and drug release (Navarro–Tumar et al., 2024).

VIII. EXAMPLE FORMULATIONS

1. Osmotic Push–Pull System of Metformin
A bilayer osmotic capsule using PEO (push polymer), HPMC, osmogen blend, and cellulose acetate membrane achieved extended release for 12 h. (Li, X, & Chen, Y. et al., 2022)

2. Swellable Elementary Osmotic Pump (SEOP) for Highly Soluble Drugs

Formulated using super-swelling polymers, NaCl osmogen, and asymmetric membrane coating to provide uniform release. (Shokri j, et al., 2020)

3. Osmotic Push–Pull Tablet of Ondansetron HCl
Used a drug suspension layer + push layer containing PEO, with CA membrane and laser-drilled orifice, giving zero-order release for 24 h. (Mehta, D., et al., 2020)

4. Push–Pull Osmotic Pump Optimized by QbD
Using Box–Behnken design, the study optimized PEO grade, osmogen amount, and membrane thickness to achieve stable release. (Khan & Bhat et al., 2021)

5. Osmotic Delivery of Enalapril Tablets
Bilayer osmotic design with HPMC, MCC, NaCl, and CA membrane, showing improved stability and controlled release. (Patil &Pawar et al., 2021)

6. Budesonide Osmotic Controlled-Release Tablets
Suitable for colon-targeted delivery using osmotic push mechanism + pH-responsive membrane modification. (Joseph, A., et al., 2021)

7. Controlled Release of Metformin via Enteric Osmotic Pump Capsule
Designed for intestinal delivery using enteric-coated semipermeable membrane + osmotic core, extending release up to 18.

8. Colloidal Osmotic Pump for Poorly Soluble Drugs
Used nano-colloidal dispersion inside an osmotic core to improve solubility and release control (Azhar et al., 2021)

9. Targeted Flexible Osmotic Device for Colon Delivery
Used pH-responsive pore-forming agents + osmotic triggers for colon-targeted drug release.
(Jungho Ha et al., 2024)

10. Floating Osmotic Pump System
A system containing gas-generating agents + osmotic core that prolonged gastric retention and sustained release. (Sultana, R., et al., 2023)

11. Multi-Component Osmotic Tablet for Anti-Hypertensive Therapy
Used bilayer osmotic structure to deliver controlled release of antihypertensive agents.
(Reed Berlet et al., 2025)

12. Osmotic Tablet Design Verified Using Machine Learning
Applied AI prediction models to optimize membrane thickness, osmotic pressure, and drug layering. (Zhang & Liu et al., 2024)

13. Asymmetric Osmotic Pump for Targeted Therapy
Phase inversion-based asymmetric membrane creating high permeability, eliminating laser drilling. (Shao et al., 2023)

14. Osmotic Tablet with Optimized Plasticizer & Polymer Ratio Used semipermeable membrane engineering for predictable release.
(Navarro-Tumar et al., 2024).

IX. EVALUATION & CHARACTERIZATION OF OSMOTIC DRUG DELIVERY SYSTEMS

1. Pre-compression properties — flow and compressibility
Measure angle of repose, bulk/tapped density, Carr's index and Hausner ratio to ensure uniform die filling and consistent tablet weight. (Khan & Bhat et al., 2021).

2. Tablet dimensions, hardness and friability
Post-compression evaluation includes thickness, diameter, hardness (crushing strength) and friability (<1% acceptable) to ensure mechanical integrity during coating and handling (Li, X, & Chen, Y.et al., 2022).

3. Content uniformity and assay
Drug content per unit is measured (usually by validated HPLC/UV methods) to confirm dose accuracy and batch consistency (Patil &Pawar et al., 2021)

4. Membrane thickness & coating weight (weight gain)
Coating level (weight gain) and uniformity are quantified since membrane thickness directly controls water influx and release rate (Navarro-Tumar et al., 2024).

5. Scanning Electron Microscopy (SEM) for surface morphology

SEM examines membrane surface, pore formation (CPOP) and orifice quality—used to confirm asymmetric membranes or nanoporous structure (Shao et al., 2020; Navarro-Tumar et al.,2024).

6. In-vitro dissolution / release testing

Dissolution performed using USP apparatus (I/II) in pH 1.2, 6.8 and water; collect time-course samples to build release profiles and assess pH-independence (Li, X, & Chen, Y.2022; Khan& Bhat et al., 2021).

7. Kinetic modelling & release mechanism

Fit dissolution data to zero-order, Higuchi, Korsmeyer Peppas etc.; true osmotic systems often show near zero-order release (Zhang, & Liu., et al., 2024).

8. Osmotic pressure measurement / osmometer testing

Measure osmotic potential of the core or osmogen solutions to correlate driving force with release rate during formulation optimization (Khan & Bhat et al., 2021).

9. Mechanical integrity after swelling

Test for deformation, cracking or membrane rupture after hydration cycles—important for SEOP and high-swelling push layers (Shokri, J., et al., 2020).

10. SEM / EDX for elemental and coating composition

Elemental mapping (EDX) combined with SEM to verify distribution of pore formers or nanoparticle additives in membranes (Navarro-Tumar et al., 2024).

11. In-vivo pharmacokinetics and IVIVC

PK studies (Tmax, Cmax, AUC) in animals/humans to confirm in-vitro-in-vivo correlation; many studies establish Level-A IVIVC for optimized ODDS (Li, X, & Chen, Y. 2022; Zhang & Liu et al., 2024).

12. Biocompatibility / irritation testing (implantables / novel materials)

For implantable or novel membrane materials, cytotoxicity and local irritation tests are required prior to long-term use (Reed Berlet et al., 2025; Navarro-Tumar et al., 2024).

13. Assay method validation & stability indicating methods

Stability-indicating HPLC methods validated for specificity, linearity, precision and robustness to quantify API and degradation products (Patil &Pawar et al., 2021).

14. Regulatory and documentation tests

Complete specification setting, stability protocol per ICH, dissolution acceptance criteria and container/closure suitability for submission (Li, X, & Chen, Y. 2022; Patil &Pawar et al., 2021)

X. RECENT ADVANCEMENTS IN OSMOTIC DRUG DELIVERY SYSTEMS

1. Nano-engineered semipermeable membranes

The hybrid organic–inorganic nanomembranes were developed, which provide extremely precise control over membrane permeability and selectivity, resulting in highly predictable drug release (Navarro-Tumar et al., 2024).

2. pH-responsive osmotic systems for colon targeting

The reported the development of colon-specific osmotic pumps that use pH-triggered poreformers, enabling targeted drug delivery for conditions like inflammatory bowel disease (Jungho Ha et al., 2024).

3. Machine learning and AI-assisted optimization

A study used AI models to predict membrane thickness, osmotic pressure, and polymer ratios, significantly reducing formulation trials (Zhang, L., et al., 2024).

4. Floating osmotic pump technology

The described an osmotic + floating hybrid system using gas-generating agents to increase gastric retention and achieve prolonged drug release (Sultana, R., et al., 2023)

5. Enteric-coated osmotic pump capsules

The Metformin Osmotic Capsule Study used enteric semipermeable coatings that allowed intestine-specific release, improving bioavailability and reducing gastric irritation (Li, X, &Chen, Y.et al., 2022)

6. Colloidal osmotic systems for poorly soluble drugs

According to nano-colloidal dispersion cores enhanced both solubility and release control for poorly soluble drugs (Azhar et al., 2021)

7. Asymmetric membrane osmotic tablets (AMOT)
The developed phase-inversion–based asymmetric membranes, which reduced laser drilling cost and improved pore uniformity (Shao et al., 2020)

8. Super-swellable polymers in SEOP
The SEOP demonstrated the use of ultra-swellable PEO polymers that generate a high osmotic driving force, enabling controlled release of low-solubility and high-dose drugs (Shokri. R., et al., 2020).

9. QbD-driven osmotic pump design
The Push–Pull QbD Study applied Design of Experiments (DoE), ANOVA, and Response Surface Methodology to scientifically optimize critical formulation and processing parameters (Khan & Bhat et al., 2021)

10. Osmotic pumps with real-time responsive membranes
next-generation membranes are being engineered to respond to temperature and ionic strength, enabling adaptive, real-time drug release modulation (Navarro-Tumar et al., 2024)

11. Enhanced stability coatings
Studies on Enalapril and Budesonide showed that low-moisture permeability cellulose acetate + plasticizer coatings improved stability and shelf-life for moisture-sensitive drugs (Patil &Pawar et al., 2021; Joseph, A., et al., 2020)

XI. APPLICATIONS OF OSMOTIC DRUG DELIVERY SYSTEMS (ODDS)

1. Chronic disease therapy requiring steady plasma drug levels
ODDS provide nearly zero-order release, making them ideal for conditions like hypertension, diabetes, and chronic pain, where fluctuation-free plasma concentration is required (ShivamGavandare et al., 2020).

2. Delivery of poorly water-soluble drugs
Push–Pull Osmotic Pumps (PPOP) and colloidal osmotic systems enhance delivery of lowsolubility drugs like budesonide, ondensetron, and similar molecules (Azhar et al., 2021; Mehta, D., et al., 2020).

3. Targeted intestinal and colon delivery
Enteric-coated osmotic capsules and pH-responsive osmotic tablets provide site-specific release to the intestine and colon—useful in inflammatory bowel disorders (Jungho Ha et al., 2024; Li, X, & Chen, Y. et al., 2022).

4. Gastro-retentive delivery (floating osmotic systems)
Floating osmotic pumps remain buoyant in the stomach, enabling prolonged gastric retention and improved bioavailability of drugs absorbed in upper GI tract (Sultana, R., et al., 2023).

5. Controlled release of high-dose drugs
SEOP and PPOP systems efficiently deliver high-dose drugs like metformin by using swellable polymers and composite osmotic layers (Li, X., Chen Y. 2022 & Shokri, j., et al., 2020).

6. Reduction of dose dumping and adverse effects
Membrane-controlled release significantly reduces peak–trough fluctuations and prevents dose dumping, increasing safety (Patil & Pawar et al., 2021).

7. Stable release for drugs sensitive to GI pH and motility
Osmotic systems provide release that is independent of GI physiology, making them suitable for drugs sensitive to pH variations (Navarro-Tumar, 2024; Shao et al., 2020)

8. Multi-drug or dual-release therapy
Advanced multilayer osmotic tablets allow delivery of two actives or two different release patterns in a single unit (Reed Berlet et al., 2025)

9. Drugs requiring colon-protective release
Budesonide and other corticosteroids used for colitis benefit from colon-targeted osmotic systems to minimize systemic exposure (Joseph, A., et al., 2021).

10. Applications in cancer therapy using micro-osmotic pumps shows micro-osmotic. delivery enabling precise long-term infusion for oncology drugs. (Reed Berlet et al., 2025)
11. Delivery of unstable molecules through protective osmotic coatings

Moisture-sensitive drugs such as enalapril show improved stability through CA–plasticizer osmotic coatings (Patil &Pawar et al., 2021)

XII. ADVANTAGES

1. Zero-order and highly predictable drug release

Osmotic systems provide constant, time-controlled release independent of drug concentration, ensuring stable plasma levels (Shivam-Gavandare et al., 2020).

2. Release independent of GI conditions

Release rate does not depend on pH, food, motility, or agitation, making them reliable across patient populations (Shao et al., 2020; Navarro-Tumar et al., 2024).

3. Suitable for both high-solubility and low-solubility drugs

EOP works efficiently for high-solubility drugs, while PPOP and colloidal osmotic pumps work for poorly soluble drugs (Azhar et al., 2021; Mehta D., 2020).

4. Reduced dose dumping and minimized side effects

Controlled membrane permeability and osmotic driving force reduce the risk of sudden drug release (Patil &Pawar et al., 2021).

5. Enhanced patient compliance

Once-daily dosing and stable therapeutic levels improve adherence in chronic disease therapy (Li, X, & Chen, Y et al., 2022).

6. High formulation flexibility

Formulation can be customized by adjusting osmotic pressure, membrane thickness, orifice diameter, and push-layer strength (Kham & Bhat et al., 2021).

7. Environmentally insensitive mechanism

Osmotic pressure remains constant irrespective of external physiological fluctuations, ensuring robustness (Navarro-Tumar et al., 2024).

8. Suitable for sustained, targeted, and extended-release applications

Osmotic pumps can be designed for gastric retention, intestinal release, or colon targeting using pH-responsive membranes (Jungho Ha et al., 2024; Sultana, R., et al., 2023).

9. Improved stability for moisture-sensitive drugs

Semipermeable coatings provide protection against humidity and oxidation (Patil &Pawar et al., 2021).

10. Highly reproducible performance

Because release is based on osmotic pressure rather than diffusion, batch-to-batch reproducibility is superior (Khan & Bhat et al., 2021).

11. Enables delivery of high-dose drugs

Bilayer systems (PPOP) and osmotic capsules can accommodate large doses like metformin (Li, X & Chen, Y. et al., 2022)

12. Low impact of formulation variability

DoE-based studies show even if excipient ratios vary slightly, osmotic systems still maintain release predictability (Zhang, & Liu, et al., 2024).

13. Long shelf-life with optimized coatings

Cellulose acetate–plasticizer membranes improve the chemical stability of sensitive APIs (Joseph, A., et al., 2021).

XIII. LIMITATIONS OF OSMOTIC DRUG DELIVERY SYSTEMS

1. Requirement of laser-drilled orifice (extra manufacturing step)

Many osmotic tablets (EOP & PPOP) need precise laser drilling, which increases equipment cost and manufacturing complexity (Shivam-Gavandare et al., 2020).

2. Risk of orifice blockage

If the drug contains poorly soluble particles, the release orifice may block, affecting release rate (Mehta, D., et al., 2020).

3. Not suitable for very insoluble drugs

Even PPOP systems struggle with extremely low-solubility APIs unless additional solubility enhancement strategies are used (Azhar et al., 2021).

4. Moisture sensitivity of osmotic core

Strong hygroscopic osmogens (NaCl, mannitol) can absorb moisture during storage, reducing stability (Patil K., et al., 2021).

5. High coating weight and time requirement

Cellulose acetate membranes require long coating times and thicker membranes, increasing production cost (Navarro-Tumar et al., 2024).

6. Specialized membrane materials required

Only specific semipermeable polymers (CA, CAP, etc.) are suitable, limiting formulation flexibility (Shao et al., 2020)

7. Limited suitability for immediate-release drugs

Osmotic systems are inherently controlled-release; fast-acting drugs may not be ideal candidates (Shivam-Gavandare et al., 2020).

8. Incompatibility between drug and push-layer polymers

High-swelling polymers (PEO, Carbopol) may interact with sensitive drugs, affecting stability (Shokri, J., et al., 2020).

9. Higher formulation and scale-up cost

Advanced systems like PPOP, floating osmotic pumps, and enteric osmotic capsules have higher material and scale-up cost (Sultana, R., et al., 2023).

10. Not suitable for drugs requiring very rapid titration

Since release is controlled and predictable, the system is not suitable for drugs where dose must be quickly adjusted (Jungho Ha et al., 2024).

11. Mechanical failure risk (membrane rupture or cracking)

Improper coating thickness, defects, or high internal osmotic pressure may cause cracking or dose dumping (Navarro-Tumar et al., 2024).

12. Large tablet size due to multilayer design

Bilayer (push–pull) tablets are larger and may be difficult for pediatric or geriatric patients to swallow (Li, X, & Chen, Y. et al., 2022).

13. Not suitable for drugs unstable in aqueous environment

Upon hydration, drug stays in solution/suspension for long duration inside system; unstable APIs may degrade (Reed Berlet et al., 2025).

14. Difficulty achieving pulsatile or multi-phase release

Simple osmotic pumps mainly offer zero-order release; complex patterns require advanced multilayer or modified membranes (Kumar, N., et al., 2024)

XIV. FUTURE PROSPECTS OF OSMOTIC DRUG DELIVERY SYSTEMS

1. Development of smart, programmable osmotic systems

next- generation osmotic membranes will be designed as stimuli-responsive systems, reacting to temperature, ionic concentration, or pH. These advanced membranes will enable programmable and adaptive drug-release profiles, aligning with emerging precision-medicine requirements (Navarro-Tumar et al., 2024).

2. AI- and machine-learning-enabled formulation optimization

The PLOS research demonstrates that artificial intelligence can accurately predict key formulation parameters such as membrane thickness, osmotic pressure, and polymer ratios. In the future, AIbased modeling is expected to support full automation and digital formulation design, improving robustness and reducing experimental workload (Zhang & Liu et al., 2024).

3. Next-generation colon- and intestine-targeted osmotic systems

The CEO highlights that future ODDS will incorporate pH-responsive pore formers and colon specific coatings, enabling precise delivery to the intestine and colon. Such innovations are particularly promising for treating inflammatory bowel disease (IBD), Crohn's disease, and ulcerative colitis (Yadav & Trivedi et al., 2024).

4. Nano-enabled osmotic pumps for poorly soluble drugs

Both are suggest that the integration of colloidal nanoparticles and nano-hybrid membranes will significantly enhance the solubility and membrane-controlled release of poorly soluble drugs, improving therapeutic outcomes (Azhar et al., 2021; Shao et al., 2020).

5. Floating–osmotic hybrid systems for gastric retention

The study indicates that future devices will combine floating technology with osmotic pumping, enabling

improved gastric retention. This hybrid approach is especially beneficial for drugs that are primarily absorbed in the upper gastrointestinal tract (Sultana, J, et al., 2023)

6. Use of biodegradable and eco-friendly semipermeable membranes

Reports from predict the development of biodegradable, eco-friendly semipermeable membranes, which reduce environmental impact while maintaining consistent osmotic performance (NavarroTumar&2024; Parmar & Ghosh et al., 2024).

7. Multi-drug and dual-release osmotic devices

Based on the multi-layer imaging work in the future will witness dual-release and step-wise release osmotic systems capable of administering multiple drugs or multiple release phases to manage chronic comorbidities (Parmar & Ghosh et al., 2024).

8. Personalized medicine through micro-osmotic devices

Future ODDS are expected to incorporate implantable micro-osmotic pumps that can deliver patient-specific doses, particularly beneficial for oncology, chronic pain management, and biologic formulations (Reed Berlet, et al., 2025).

9. QbD- and digital-twin-based manufacturing systems

The PPOP QbD study indicates that future pharmaceutical manufacturing will adopt digital twins, real-time release testing (RTRT), and automated process controls, significantly enhancing reproducibility and regulatory compliance (Khan & Bhat et al., 2021).

10. Improved stability systems for moisture-sensitive drugs

Studies on enalapril and budesonide osmotic tablets suggest that advanced ultra-low-moisture cellulose acetate coatings will enhance the long-term stability of hygroscopic or moisture-sensitive molecules (Patil &Pawar, 2021; Joseph et al., 2021).

11. Expansion toward biologics and peptide delivery

Advancements in micro-osmotic pump technology suggest promising applications in delivering peptides and biologics with sustained precision, making it a major future direction in targeted therapy (Parmar & Ghosh, 2024).

12. Development of combination osmotic + transdermal or hydrogel systems

Emerging research also points toward hybrid delivery platforms, such as osmotic–hydrogel or osmotic–microneedle systems, which may offer improved control and enhanced patient compliance (Navarro-Tumar et al., 2024)

XV. CONCLUSION

Osmotic drug delivery systems have emerged as one of the most dependable and intelligent platforms for sustained and targeted therapeutic delivery. Their unique osmotic pressure–driven mechanism ensures zero-order release, minimal influence of gastrointestinal variability, and consistent plasma drug levels, making them highly advantageous for chronic disease management Modern osmotic designs—including Push–Pull Osmotic Pumps (PPOP), Controlled-Porosity Osmotic Pumps (CPOP), SEOP devices, and enteric osmotic capsules—have expanded the applicability of osmotic systems to both highly soluble and poorly soluble drugs, overcoming several limitations of traditional extended-release technologies

Recent advancements from highlight significant transformation in ODDS using nano-engineered membranes, asymmetric coatings, colloidal osmotic cores, and floating osmotic systems, which enable improved release precision, enhanced solubility, and superior therapeutic outcomes Emerging innovations such as pH-responsive, colon-targeted osmotic systems and AI-driven formulation optimization further strengthen the potential of ODDS as next-generation controlled release technologies

Although osmotic pumps exhibit remarkable benefits, they continue to face challenges such as manufacturing complexity, higher coating weight requirements, moisture sensitivity, and limitations in delivering extremely insoluble or unstable drugs Addressing these limitations through smart materials, eco-friendly membranes, digitalized QbD approaches, and advanced computational modeling will pave the way for more efficient, patient-specific, and clinically impactful osmotic systems in the future.

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