JOURNAL OF PHARMA INSIGHTS AND RESEARCH ISSN NO. 3048-5428

REVIEW ARTICLE

A Review on Controlled Porosity Osmotic Drug Delivery Systems

Voleti Vijaya Kumar[1], Ismail Y*[2]

[1] *Research Scholar, Crescent School of Pharmacy, B.S. Abdur Rahman Crescent Institute of Science and Technology, Vandalur, Chennai, Tamil Nadu, India*
[2] *Associate Professor, Crescent School of Pharmacy, B.S. Abdur Rahman Crescent Institute of Science and Technology, GST Road, Vandalur, Chennai, Tamil Nadu, India*

Publication history: Received on 16th Dec 2024; Revised on 26th Dec 2024; Accepted on 28th Dec 2024

Article DOI: 10.69613/anw6kz52

Abstract: Controlled porosity osmotic drug delivery systems (CPODS) represent a significant advancement in pharmaceutical technology, offering precise control over drug release rates through osmotic mechanisms. These systems utilize semipermeable membranes with controlled porosity to achieve sustained drug delivery, addressing limitations of conventional dosage forms. The fundamental principle involves water penetration through the semipermeable membrane, creating an osmotic gradient that facilitates drug release through formed micropores. CPODS demonstrate numerous advantages, including zero-order drug release kinetics, reduced dosing frequency, improved patient compliance, and minimized first-pass metabolism. The drug release is governed by various parameters such as osmotic pressure, membrane permeability, and pore characteristics, which can be optimized to achieve desired therapeutic outcomes. Recent developments have eliminated the need for mechanical drilling of delivery orifices, instead utilizing pore-forming agents that create micropores in situ. The system's effectiveness depends on critical components including osmotic agents, semipermeable membranes, pore-forming agents, and plasticizers. This innovative technology has shown particular promise in delivering both water-soluble and poorly soluble drugs, maintaining consistent plasma concentrations over extended periods. The robust in vitro-in vivo correlation and independence from physiological factors make CPODS an attractive platform for controlled drug delivery applications. As research continues, these systems show potential for expanding into novel applications such as pulsatile delivery and multi-drug therapy.

Keywords: Controlled porosity osmotic pump; Semipermeable membrane; Zero-order release; Osmotic pressure; Sustained drug delivery.

1. Introduction

Drug delivery systems have evolved significantly over the past decades, transitioning from conventional immediate-release formulations to more sophisticated controlled-release systems. The oral route remains the most preferred path for drug administration due to its convenience, cost-effectiveness, and high patient compliance [1]. However, conventional oral drug delivery systems often face challenges such as unpredictable absorption profiles and fluctuating drug plasma levels [2]. The advancement in pharmaceutical technology has led to the development of novel drug delivery systems (NDDS), which offer superior control over drug release kinetics. Among these, osmotic drug delivery systems have emerged as a promising approach, utilizing osmotic pressure as the driving force for controlled drug release [3]. These systems have garnered significant attention due to their ability to maintain constant drug levels in the blood, thereby maximizing therapeutic efficiency while minimizing side effects [4]. Controlled porosity osmotic drug delivery systems (CPODS) represent a significant advancement in osmotic technology. Unlike traditional osmotic systems that require mechanical drilling of delivery orifices, CPODS employ specially designed polymeric membranes that develop controlled porosity in the gastrointestinal environment [5]. This innovative approach not only simplifies manufacturing but also provides more uniform drug release characteristics [6].

The fundamental principle of CPODS involves the creation of an osmotic gradient across a semipermeable membrane. When the system encounters aqueous fluids in the gastrointestinal tract, water penetrates through the membrane, dissolving the drug and creating internal pressure that forces the drug solution out through the formed micropores [7]. This process continues at a controlled rate, largely independent of physiological variables such as pH, enzymatic activity, and gastrointestinal motility [8]. One of the most significant advantages of CPODS is their ability to deliver drugs following zero-order release kinetics, where the drug release rate remains constant over time [9]. This characteristic is particularly beneficial for drugs requiring sustained plasma levels or those with

* Corresponding author: Ismail Y

narrow therapeutic windows [10]. Moreover, these systems can accommodate both highly water-soluble and poorly soluble drugs, making them versatile platforms for drug delivery [11]. The success of CPODS depends on careful consideration of various formulation parameters, including membrane composition, osmotic agents, and pore-forming materials. Recent research has focused on optimizing these components to enhance system performance and expand the range of suitable drug candidates [12].

2. Controlled Porosity Osmotic Pump (CPOP)

2.1. Design and Structure

CPOP represents a sophisticated advancement in osmotic drug delivery technology, characterized by its unique asymmetric membrane coating. The system consists of a core tablet containing the active pharmaceutical ingredient and osmotic agents, surrounded by a semipermeable membrane formed through a phase inversion process [13]. This membrane's distinctive feature lies in its controlled porosity, which develops when the dosage form encounters aqueous media in the gastrointestinal tract [14].

2.2. Mechanism of Drug Release

The drug release mechanism from CPOP is governed by osmotic principles. Upon contact with aqueous media, water penetrates through the semipermeable membrane due to the osmotic gradient created by the osmogenic agents in the core. This water influx leads to the dissolution of soluble components within the core tablet. The resulting hydrostatic pressure forces the drug solution through the micropores that form in the membrane coating [15]. The rate of drug release is primarily controlled by the osmotic pressure difference across the membrane and the membrane's permeability characteristics [16].

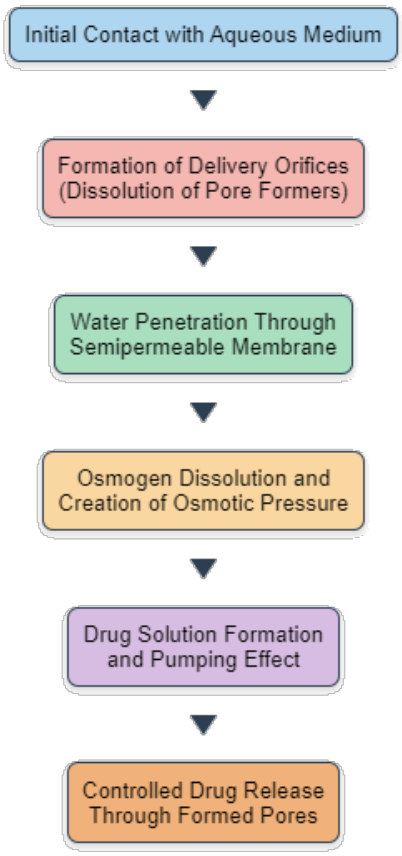

Figure 1. Mechanism of drug release from CPOP system

2.3. Advantages of CPOP Technology

The CPOP system offers several significant benefits over conventional drug delivery systems. The primary advantage is the achievement of zero-order drug release kinetics, which ensures consistent plasma drug levels over extended periods. Additionally, the system demonstrates remarkable independence from gastrointestinal pH variations and motility patterns, leading to more predictable drug absorption profiles [17].

2.4. Role of Membrane Formation

The formation of the semipermeable membrane is crucial in CPOP technology. The phase inversion process results in an asymmetric membrane structure with controlled pore size distribution. This structure is essential for maintaining the desired water influx rate while preventing the passage of larger drug molecules through the membrane itself [18]. The membrane's characteristics can be modified by adjusting the composition of the coating solution and the conditions during the phase inversion process.

2.5. Factors Influencing Drug Release

Several key factors influence the performance of CPOP systems:

2.5.1. Membrane Permeability

The water permeability of the semipermeable membrane directly affects the rate of osmotic pump activation and subsequent drug release [19].

2.5.2. Osmotic Pressure Gradient

The difference in osmotic pressure between the core and external environment drives the water influx and drug release process [20].

2.5.3. Core Formulation

The composition of the core tablet, including the nature and concentration of osmotic agents, influences the overall system performance [21].

2.5.4. Environmental Conditions

While the system is relatively independent of physiological conditions, extreme variations in external environment can affect its performance [22].

2.6. Applications in Drug Delivery

CPOP technology has demonstrated particular utility in developing controlled-release formulations for various therapeutic agents. The system is especially beneficial for drugs requiring precise release rates and those with narrow therapeutic windows. Recent applications have expanded to include modified release formulations for both water-soluble and poorly soluble drugs [23].

Table 1. Critical Parameters Affecting CPOP Performance and Their Impact on Drug Release

Parameter	Acceptable Range	Impact on Drug Release	Optimization Strategy
Membrane Thickness	200-500 μm	Directly proportional to release rate	Adjust coating process parameters
Pore Former Concentration	20-50% w/w	Controls membrane porosity	Balance with mechanical strength
Osmogen Concentration	30-60% w/w	Determines osmotic pressure	Optimize based on drug solubility
Core Hardness	4-8 kg/cm²	Affects water penetration rate	Adjust compression force
Plasticizer Content	10-30% w/w	Influences membrane flexibility	Balance with mechanical properties
Water Permeability	$1\text{-}5 \times 10^{-4}$ cm/h	Controls water influx rate	Select appropriate membrane material
Pore Size	5-50 μm	Affects drug diffusion rate	Control phase inversion process
Drug Loading	20-40% w/w	Influences release duration	Balance with osmogen content
Coating Solution Viscosity	50-200 cP	Affects membrane formation	Adjust polymer concentration
Environmental pH	1.2-7.4	Minimal effect on release	Design pH-independent system

3. Essential components of osmotic systems

3.1. Drug Selection Criteria

The selection of appropriate drug candidates for osmotic delivery systems requires careful consideration of various physicochemical properties. Ideal candidates typically demonstrate moderate water solubility and suitable biological half-lives. Drugs requiring

prolonged treatment regimens, such as antihypertensives, antidiabetics, and anti-inflammatory agents, are particularly well-suited for osmotic delivery systems [24]. The system has successfully incorporated various drugs including nifedipine, diltiazem hydrochloride, metoprolol, glipizide, and carbamazepine [25].

Table 2. Examples of Drugs Formulated as Controlled Porosity Osmotic Pump Systems

Drug	Therapeutic Category	Solubility (mg/mL)	Half-life (hrs)	Clinical Application
Nifedipine	Antihypertensive	0.0058	2-5	Once-daily control of hypertension
Diltiazem HCl	Calcium Channel Blocker	465	3-4.5	Management of angina
Glipizide	Antidiabetic	0.078	2-4	Type 2 diabetes control
Metoprolol	Beta-blocker	120	3-7	Hypertension management
Propranolol	Beta-blocker	50	3-6	Anxiety and hypertension
Ketoprofen	NSAID	0.13	1.8-2	Pain management
Pseudoephedrine	Decongestant	250	5-8	Nasal congestion
Verapamil HCl	Calcium Channel Blocker	83	4-7	Arrhythmia treatment
Carbamazepine	Anticonvulsant	0.017	25-65	Epilepsy management
Theophylline	Bronchodilator	8.3	8-9	Asthma control

3.2. Osmotic Components

Osmotic agents, or osmogens, play a crucial role in establishing and maintaining the osmotic gradient necessary for drug release. These compounds generate controlled osmotic pressure when dissolved in aqueous media. Common osmotic agents include inorganic salts such as sodium chloride, potassium chloride, and magnesium sulfate, as well as organic compounds like mannitol, sorbitol, and glucose. The selection of osmotic agents depends on their compatibility with the drug and their ability to generate appropriate osmotic pressure [26].

3.2.1. Semipermeable Membrane

The semipermeable membrane serves as the rate-controlling barrier in osmotic systems. Key requirements for membrane materials include:

- Chemical inertness and stability
- Sufficient rigidity to maintain structural integrity
- Controlled water permeability
- Biocompatibility

Cellulose acetate derivatives remain the most widely used materials for semipermeable membranes, offering excellent film-forming properties and controllable water permeability [27].

3.3. Water-Penetrating Agents

Water-penetrating agents, also known as wicking agents, facilitate water transport throughout the tablet core. These materials create a network of channels that enhance surface area for drug dissolution and release. Common wicking agents include polyvinylpyrrolidone (PVP), sodium lauryl sulfate (SLS), and microcrystalline cellulose. The selection of wicking agents significantly influences the drug release pattern and overall system efficiency [28].

3.4. Pore-Forming Agents

Pore-forming agents are essential components that create the controlled porosity characteristic of these systems. During membrane formation, these agents become incorporated into the coating and subsequently dissolve upon contact with aqueous media, creating a network of micropores. Various water-soluble polymers, low molecular weight compounds, and volatile substances serve as effective pore-forming agents. The concentration and type of pore-forming agent directly influence the final membrane porosity and drug release kinetics [29].

3.5. Plasticizers

Plasticizers are incorporated into the membrane formulation to modify its mechanical properties and permeability characteristics. These additives reduce the glass transition temperature of the polymer, improving film formation and flexibility. Common plasticizers include:

- Polyethylene glycols
- Dibutyl phthalate
- Triethyl citrate
- Propylene glycol

The selection and concentration of plasticizers significantly impact membrane formation, mechanical strength, and drug release properties [30]

4. Conclusion

Controlled porosity osmotic drug delivery systems represent a significant advancement in pharmaceutical technology, offering precise control over drug release kinetics. These systems successfully address many limitations of conventional dosage forms by providing consistent drug release patterns independent of physiological variables. The elimination of mechanical drilling through the use of in-situ pore formation has simplified manufacturing processes while maintaining therapeutic efficiency. Recent developments in formulation components, including advanced membrane materials and novel osmotic agents, have expanded the applicability of these systems to a broader range of drug molecules. The versatility of CPODS in accommodating both water-soluble and poorly soluble drugs, combined with their excellent in vitro-in vivo correlation, positions them as a promising platform for future drug delivery applications.

References

[1] Pather SI, Russell I, Syce JA, Neau SH. Sustained release theophylline tablets by direct compression: Part 1: formulation and in vitro testing. Int J Pharm. 1998;164(1-2):1-10.

[2] Zhang H, Zhang J, Streisand JB. Oral mucosal drug delivery: clinical pharmacokinetics and therapeutic applications. Clin Pharmacokinet. 2002;41(9):661-80.

[3] Verma RK, Krishna DM, Garg S. Formulation aspects in the development of osmotically controlled oral drug delivery systems. J Control Release. 2002;79(1-3):7-27.

[4] Santus G, Baker RW. Osmotic drug delivery: a review of the patent literature. J Control Release. 1995;35(1):1-21.

[5] Thombre AG, Cardinal JR, DeNoto AR, Herbig SM, Smith KL. Asymmetric membrane capsules for osmotic drug delivery. J Control Release. 1999;57(1):65-73.

[6] Verma RK, Garg S. Development and evaluation of osmotically controlled oral drug delivery system of glipizide. Eur J Pharm Biopharm. 2004;57(3):513-25.

[7] Liu L, Ku J, Khang G, Lee B, Rhee JM, Lee HB. Nifedipine controlled delivery by sandwiched osmotic tablet system. J Control Release. 2000;68(2):145-56.

[8] Theeuwes F. Elementary osmotic pump. J Pharm Sci. 1975;64(12):1987-91.

[9] Bindschaedler C, Gurny R, Doelker E. Osmotically controlled drug delivery systems produced from organic solutions and aqueous dispersions of cellulose acetate. J Control Release. 1986;4(3):203-12.

[10] Jensen JL, Appel LE, Clair JH, Zentner GM. Variables that affect the mechanism of drug release from osmotic pumps coated with acrylate/methacrylate copolymer latexes. J Pharm Sci. 1995;84(5):530-3.

[11] Verma RK, Mishra B, Garg S. Osmotically controlled oral drug delivery. Drug Dev Ind Pharm. 2000;26(7):695-708.

[12] Rani M, Mishra B. Comparative in vitro and in vivo evaluation of matrix, osmotic matrix, and osmotic pump tablets for controlled delivery of diclofenac sodium. AAPS PharmSciTech. 2004;5(4):71-9.

[13] Prakash RB, Geetha T, Purushothaman M, Raghunathan P. Optimization and characterization of controlled porosity osmotic pump tablets of diltiazem hydrochloride. Drug Dev Ind Pharm. 2009;35(1):95-104.

[14] Theeuwes F, Swanson DR, Guittard G, Ayer A, Khanna S. Osmotic delivery systems for the beta-adrenoceptor antagonists metoprolol and oxprenolol: design and evaluation of systems for once-daily administration. Br J Clin Pharmacol. 1985;19(2):69S-76S.

[15] Herbig SM, Cardinal JR, Korsmeyer RW, Smith KL. Asymmetric-membrane tablet coatings for osmotic drug delivery. J Control Release. 1995;35(2-3):127-36.

[16] Thombre AG, Appel LE, Chidlaw MB, Daugherity PD, Dumont F, Evans LA, Sutton SC. Osmotic drug delivery using swellable-core technology. J Control Release. 2004;94(1):75-89.

[17] Verma RK, Garg S. Current status of drug delivery technologies and future directions. Pharm Technol. 2001;25(2):1-14.

[18] Zentner GM, Rork GS, Himmelstein KJ. The controlled porosity osmotic pump. J Control Release. 1985;1(4):269-82.

[19] Wong PSL, Barclay B, Deters JC, Theeuwes F. Osmotic device with dual thermodynamic activity. J Pharm Sci. 1986;75(10):926-33.

[20] Ghosh T, Ghosh A. Drug delivery through osmotic systems: An overview. J App Pharm Sci. 2011;1(2):38-49.

[21] Malaterre V, Ogorka J, Loggia N, Gurny R. Oral osmotically driven systems: 30 years of development and clinical use. Eur J Pharm Biopharm. 2009;73(3):311-23.

[22] Rose S, Nelson JF. A continuous long-term injector. Aust J Exp Biol Med Sci. 1955;33(4):415-20.

[23] Ali J, Qureshi J, Ali N, Ghilzai NK. Development and in vitro evaluation of controlled porosity osmotic pump-based drug delivery system of metoprolo succinate. Trop J Pharm Res. 2013;12(2):123-8.

[24] Mc Clelland GA, Sutton SC, Engle K, Zentner GM. The solubility-modulated osmotic pump: in vitro/in vivo release of diltiazem hydrochloride. Pharm Res. 1991;8(1):88-92.

[25] Keraliya RA, Patel C, Patel P, Keraliya V, Soni TG, Patel RC, Patel MM. Osmotic drug delivery system as a part of modified release dosage form. ISRN Pharm. 2012;2012:528079.

[26] Liu L, Khang G, Rhee JM, Lee HB. Monolithic osmotic tablet system for nifedipine delivery. J Control Release. 2000;67(2-3):309-22.

[27] Babu CA, Prasad MS, Ramana Murthy KV. Controlled-porosity osmotic pump tablets-an overview. J Pharm Res Health Care. 2010;2(1):114-26.

[28] Bindschaedler C, Gurny R, Doelker E. Mechanically strong films produced from cellulose acetate latexes. J Pharm Pharmacol. 1987;39(5):335-8.

[29] Hashem FM, Shaker DS, Ghorab MK, Nasr M, Ismail A. Formulation, characterization, and clinical evaluation of microemulsion containing clotrimazole for topical delivery. AAPS PharmSciTech. 2011;12(3):879-86.

[30] Guan J, Zhou L, Nie S, Yan T, Tang X, Pan W. A novel gastric-resident osmotic pump tablet: in vitro and in vivo evaluation. Int J Pharm. 2010;383(1-2):30-6