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Review Article

Osmotic Drug Delivery System - A Review

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Abstract

The discovery of new drugs delivery systems is the key to pharmaceutical research and development. To control or modify the distribution of the medication over an extended period of time, numerous conventional drug delivery systems have been developed. A tailored delivery of medications is not possible with older drug delivery techniques. Additionally, the bioavailability of the drugs was also influenced by the internal environment of our body. Extensive research was done on how to deliver pharmaceutical medications to a specific location and have them be effective for a long time in order to treat chronic disorders like diabetes, hypertension, etc. This was made feasible by medications that are released in a controlled rhythm and last for a long time, producing the desired effect. The most successful way for delivering medications in a controlled manner is osmotic distribution. By using this technique, it may be possible to deliver the medication at the desired location for a considerable amount of time while avoiding the impact of the gastrointestinal pH and other physiological variables. Osmotic medication administration reduces dosage frequency, increasing patient compliance and treatment adherence. Osmogens and semi-permeable membranes are used in this system, which uses the osmosis principle to control drug delivery through orifices. The fundamental osmotic pressure theory is used by the osmotic drug delivery system (ODDS) for regulating drug release to minimise side effects and keep drug concentration within the therapeutic window. Osmosis is a physical phenomenon that has been widely studied by researchers in many branches of science and engineering. Osmotic devices are the foundation of the strategy-based method for controlled drug administration that is most promising. The majority of the time, conventional pharmaceutical delivery is unable to regulate medication release or effective concentration at the target site. The plasma concentration may fluctuate as a result of this type of dosage strategy. Osmosis is a procedure that allows drugs to be given in a regulated manner over an extended period.

Keywords: Osmosis; Osmotic; Delivery; Controlled Drug Delivery; Novel Drug Delivery System

Introduction

The oral route remains the most preferred method for drug administration due to its extensive active surface area. However, traditional oral drug delivery systems often lack control over drug release, leading to fluctuating drug concentrations in the plasma and subsequent side effects. Variability in drug absorption from conventional dosage forms arises from multiple factors including excipients, drug physicochemical properties, and physiological variables such as pH and motility of the gastrointestinal tract. Uncontrolled fast medication release may result in local gastrointestinal or systemic toxicity [1]. To overcome these limitations, various approaches, including sustained/controlled drug delivery systems, have been developed across different administration routes. Controlled-release delivery techniques encompass transdermal, intravenous, and oral methods, with oral osmotically controlled release (OOCR) delivery devices utilizing osmotic pressure to achieve controlled drug distribution. The rate and extent of drug release from such systems are influenced by both drug and system characteristics, offering opportunities for optimization to achieve desired release profiles [2].

Since the creation of an implanted pump by Australian Physiologists Rose and Nelson in 1955, osmotic medication delivery technology has advanced significantly. Osmotic drug delivery systems utilize osmogens to achieve regulated medication distribution for up to 10-16 hours, a well-established method in both veterinary and human medicine. While oral drug delivery systems offer rapid drug release, they often lack control over sustained drug release and maintaining effective concentrations at the target site [3]. Previous discussions have explored one and two compartment osmotic drug delivery systems. Osmotically regulated drug delivery devices enable both systemic and targeted drug delivery, independent of gastrointestinal tract physiology, utilizing osmotic pressure for controlled drug release. Osmotic Pump Controlled Release Preparation is a distinctive drug delivery system leveraging the osmotic pressure difference across a semi-permeable membrane as its primary control mechanism. Osmosis, the natural movement of solvent across a semi-permeable membrane, drives this process, with osmotic pressure regulating solvent flow based on solute concentration differentials [4].

Recent interest in novel drug delivery systems (NDDS) has focused on osmotically regulated drug delivery systems (ODDS), which utilize osmotic pressure for controlled drug delivery. Unlike traditional oral controlled release dosage forms, drug release from osmotic mechanisms remains unaffected by stomach pH or motility. However, factors such as pH, gastrointestinal (GI) motility, and food presence in the GI tract may influence medication release from oral controlled release dosage forms [5]. Osmotically controlled drug delivery systems (OCDDS) represent a promising technology due to their independent drug release mechanism from pH and hydrodynamic conditions, ensuring a high degree of in vitro/in vivo correlation. Osmosis, the process of solvent movement through a semipermeable membrane, drives drug delivery by utilizing osmotic pressure differences. The Osmotic Pump Controlled Release Preparation stands as a revolutionary drug delivery device, leveraging osmotic pressure to control drug release rates. Recent advancements include osmotic tablets with leachable coatings that create delivery apertures upon contact with water, enabling osmotic pumping systems to regulate medication release. These innovations underscore the potential of osmotic drug delivery systems in providing precise and controlled drug release mechanisms [6].

The purpose of the article

The purpose of the article is to emphasize the importance of developing new drug delivery systems in pharmaceutical research and development. It highlights the limitations of conventional drug delivery techniques in controlling or modifying the distribution of medication over time and in specific locations within the body. The article stresses the need for tailored drug delivery methods, especially for treating chronic disorders like diabetes and hypertension. The article introduces osmotic drug delivery systems (ODDS) as a promising approach for controlled drug administration. ODDS utilizes the principle of osmosis to regulate drug release over an extended period, thereby minimizing side effects and maintaining drug concentration within the therapeutic window. By incorporating osmogens and semi-permeable membranes, ODDS can deliver medication at the desired location for a considerable duration, overcoming the influence of physiological variables like gastrointestinal pH.

Furthermore, the article discusses recent advancements in osmotic drug delivery systems, including the integration of microchip technology and sensors. These innovations enhance precision in drug delivery and enable real-time monitoring of physiological parameters, thereby improving treatment outcomes and patient compliance. Overall, the article aims to highlight the significance of developing innovative drug delivery systems, particularly osmotic-based approaches, in improving the effectiveness and safety of pharmaceutical treatments for chronic disorders.

Principle of osmotic drug delivery system [3]

Osmotic Drug Delivery System driven through the “Osmotic Pressure”. Osmotic pressure is a colligative feature that is reliant on the concentration of the solute that it is created from solutions with the same solvent and solute system but varying concentrations display an osmotic pressure proportional to their concentrations. By maintaining a steady osmotic pressure, an osmotic medication delivery system may maintain a constant water inflow [7]. The medicine releases at a steady rate of zero order as a result. These systems are excellent for the delivery of medications with modest water solubility since the rate of drug release from an osmotic pump depends on both the osmotic pressure of the core and the solubility of the medication [8].

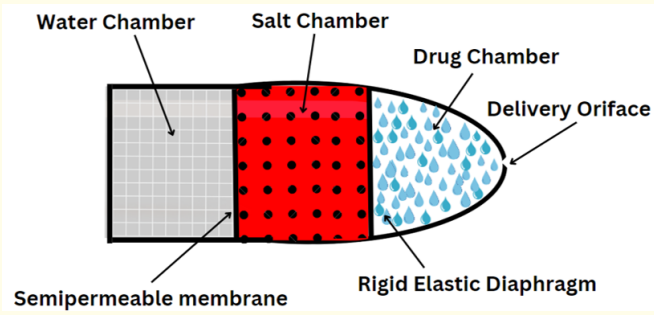

Figure 1: Different components of Osmotic Drug Delivery System.

Osmotic pressure equation ($\pi = n2\ RT$) provides a fundamental understanding of the underlying principle behind osmosis, which is crucial for comprehending osmotic drug delivery systems. However, merely mentioning the equation may not fully convey its significance in the context of drug delivery. Therefore, it's important to elaborate on how the variables in the equation affect osmosis and, consequently, the performance of osmotic drug delivery systems [9].

- π (Osmotic Pressure): Osmotic pressure is directly proportional to the concentration of solute particles (n), the temperature (T), and the gas constant (R), while inversely proportional to the volume of the solution. In osmotic drug delivery systems, manipulating osmotic pressure is key to controlling drug release rates. By adjusting the concentration of osmogens or solute particles within the system, pharmaceutical engineers can regulate osmotic pressure to achieve desired drug release profiles.
- **n (Number of Solute Particles):** The number of solute particles dissolved in the solution directly influences osmotic pressure. In osmotic drug delivery systems, the choice and concentration of osmogens play a crucial role in determining the osmotic pressure gradient across the semi-permeable membrane. This gradient drives water influx into the system, leading to controlled drug release.
- **T (Temperature):** Temperature affects osmotic pressure through its influence on the kinetic energy of solvent molecules. Higher temperatures generally result in increased kinetic energy and, consequently, higher osmotic pressure. Pharmaceutical researchers must consider the temperature sensitivity of osmotic drug delivery systems during formulation and storage to ensure consistent performance under varying environmental conditions.
- **R (Gas Constant):** The gas constant represents the relationship between pressure, volume, temperature, and the number of moles of gas. While it doesn't directly influence osmosis, it is a constant factor in the osmotic pressure equation. Understanding its role helps in designing osmotic drug delivery systems with precise control over drug release kinetics.

In the osmotic drug delivery system, drug release occurs at a steady rate of zero order. This is achieved through a controlled process where osmotically active solutes inside the drug reservoir create an osmotic pressure gradient, drawing water into the reservoir. As water enters, it builds up hydrostatic pressure, leading to a constant expulsion of the drug solution through a delivery port. This zero-order kinetics ensures a predictable release profile, maintaining optimal drug concentrations in the body over time and improving patient compliance [10].

Formulation aspects

The preparation features that distract the distribution of medication after osmotic system through oral route remain by way of follows:

Delivery orifice

Each osmotic device contains at least one opening where medication can be dispensed. The size of the distribution aperture must be changed primarily to control the osmotic device's medication delivery. For the correct discharge of the medication, the aperture's dimensions shouldn't be either too large or too small [11]. The dimensions have an impact on the release rate because they change the water pressure inside the system. If the aperture's size is extremely small, a strong internal pressure will develop that could harm the membrane. Aperture diameters should be between 0.075 and 0.274 mm. The speed at which the medication releases will not be controlled if the dimension is larger than or equal to 0.368 mm [12]. Different techniques are employed to achieve aperture. Puncturing mechanically is one approach [13]. Another popular technique is laser puncturing. In the laser approach, the device surface is exposed to a laser beam, which causes it to absorb energy, heat up, and produce an aperture. We can modify the aperture diameters by varying the laser ray power. None of the devices need that the wall be pierced. Some people can create their own apertures [14]. These gadgets include pore formers that can dissolve in water.

They dissolve when they meet water, creating an opening.

Methods of creating a delivery orifice in the osmotic tablet coating are:

- **Mechanical drill:** With this technique, an aperture is created mechanically. When all the material has been dissolved, leaving the hollow shell left, the hole dimension and film width are measured under a microscope.
- **Laser drill:** This method is used to create apertures of extremely small size. Usually, CO2 laser ray (wavelength of 10.6 nm) is useful for us, through which excellent reliability features are acquired at low costs [15]. Water can only enter via the wall, so when it does, the outside part of the device liquefies. Pressure is created across the membrane as a result of this.

Solubility

Solubility is a factor that plays a significant role in osmotic systems like EOP. A medication with a ≤0.05 g/cm2 solubility would release ≥95% of the substance. Many medications' intrinsic water solubility may prevent them from fusing in an osmotic system of EOP. A good concentration range for the osmotic system is 50–300 mg/ml [16].

Membrane thickness

The breadth of the selective membrane is a key factor in regulating water entry. Drug release can be controlled and altered up to 1000 times by changing the makeup of the film.

Evaluation

The following are the evaluation criteria:

- **Hardness:** Using a Scheleuniger tablet hardness tester, the diameter and crushing strength of a randomly chosen tablet were assessed.
- **Friability test:** Twenty tablets from each formulation were put in a Roche friabilator and rotated for four minutes. After that, the tablet was reduced and reweighed. The friability was determined as a weight loss percentage.
- **Effect of pH:** An in vitro investigation is conducted in various mediums to determine the impact of pH on formulation development.
- **Osmotic pressure effect:** To determine how osmotic pressure affects formulation, release mechanism studies are conducted at various pressures.
- ***In-vitro* testing:** The traditional USP paddle and basket type of device is used for in vitro drug release from the oral osmotic system. The standard specifications, which are followed for oral controlled drug delivery systems and are equivalently applicable for oral osmotic pumps, have been used for dissolution media, which are typically distilled water as well as simulated gastric fluid (for the first 2-4 hours) and intestinal fluids (for the following hours) [17].

Recent advancements in osmotic drug delivery systems

Recent advancements in osmotic drug delivery systems have seen the integration of microchip technology and sensors to enhance drug delivery precision and monitoring. These innovations offer improved control over drug release profiles and enable real-time monitoring of various physiological parameters. Here are some recent advancements.

Wireless osmotic drug delivery systems

Some advanced osmotic drug delivery systems incorporate wireless communication capabilities, allowing healthcare providers to remotely monitor patient adherence and response to treatment. This enables timely intervention and optimization of therapy without the need for frequent clinic visits.

Closed-loop systems

Closed-loop osmotic drug delivery systems use feedback control algorithms to adjust drug release rates based on continuous monitoring of physiological parameters. These systems offer the potential for personalized therapy optimization and improved patient outcomes.

Wireless Osmotic MicroCHIPS

The first human trial of an implanted microchip, developed by MicroCHIPS Inc., aimed to release a drug for osteoporosis in response to wireless signals. The microchip, with 20 pinprick-sized reservoirs, each containing a dose of the drug, demonstrated promising results in delivering the drug once daily without the need for repeated injections. Human parathyroid hormone fragment (1–34)

[hPTH(1–34)] was used as the drug, which typically requires burdensome daily injections.

Implantation of the microchip, which can be performed under local anesthesia in a doctor's office, was well-tolerated by patients, with no reported toxic or adverse effects. Pharmacokinetic profiles of the drug delivery were similar to subcutaneous injections, indicating the efficacy of the device. However, there was one instance of device failure in a patient not included in the analysis.

Despite the promising results, the technology is still in the development phase, and it may take several years to gain approval from regulatory authorities such as the U.S. Food and Drug Administration (FDA) [18,19].

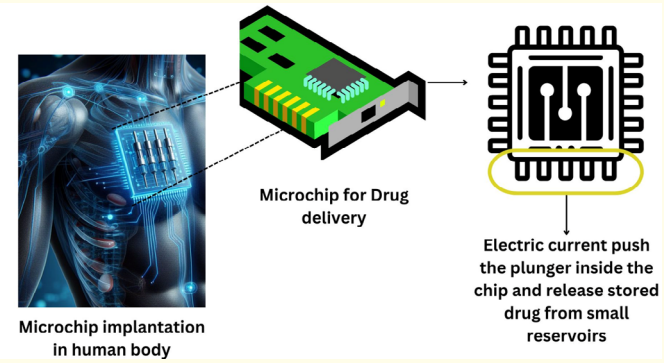

Figure 2: Drug delivery from wireless Osmotic microchip.

Smart osmotic drug delivery devices

Osmotic drug delivery devices equipped with sensors can monitor various physiological parameters such as pH, temperature, or biomarkers indicative of disease progression. These sensors provide feedback to the device, allowing it to adjust drug release rates in real-time based on the patient's condition.

The LiRIS® device

The LiRIS® device employs a double lumen medical-grade PDMS (polydimethylsiloxane) tube. One lumen contains lidocaine tablets, while the other houses a shape-memory wire made of nitinol. Insertion and retrieval from the bladder are performed through standard nonsurgical procedures such as catheterization or cystoscopy [20].

The device's design allows for easy deformation into a linear shape for insertion and then returns to its pretzel-like shape once inserted. Its compact size, akin to a paper clip, prevents expulsion during urination and minimizes the risk of injury or inflammation.

Once inside the bladder, the silicone tube acts as a semi-permeable membrane, while a small laser-drilled orifice in the tube's wall serves as the outlet for lidocaine release. This setup enables controlled and prolonged delivery of lidocaine directly to the bladder lining, offering relief to patients suffering from interstitial cystitis and related conditions.

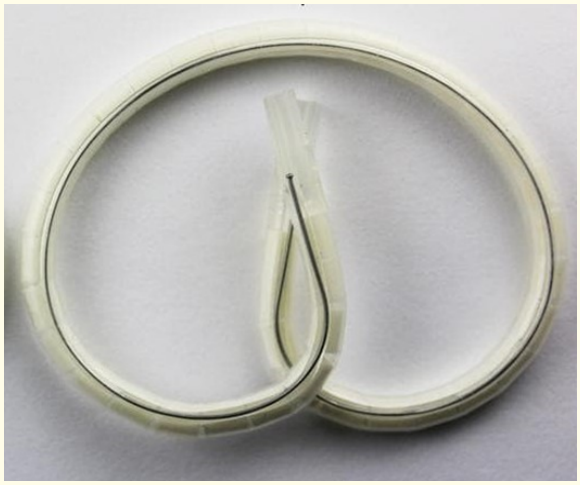

Figure 3: Drug delivery from The LiRIS® device (Smart osmotic device).

Beyond interstitial cystitis, the LiRIS® device is being explored for treating patients undergoing ureteral stent placement after kidney stone removal. Future applications of this technology platform may include delivering chemotherapy for bladder cancer, managing overactive bladder, and addressing various other bladder diseases, though these are currently in pre-clinical stages of development.

In a significant development, TARIS Biomedical's LiRIS program was acquired by Allergan in 2014 for nearly $600 million. This acquisition underscores the recognition of LiRIS as a valuable asset in addressing unmet medical needs in the treatment of IC/BPS.

Additionally, Medtronic's Synchromed® Infusion Pump System, designed to deliver baclofen for muscle spasticity, represented an-

other notable advancement in drug delivery technology it faced challenges and was recalled in 2015 due to manufacturing compliance issues and concerns regarding patient safety [21].

Implantable osmotic pumps with sensing capabilities

Implantable osmotic pumps with integrated sensors enable continuous drug delivery while simultaneously monitoring relevant physiological parameters. These systems offer a minimally invasive approach to long-term drug delivery and monitoring, particularly suitable for chronic conditions requiring precise medication management.

Overall, the integration of microchip technology and sensors into osmotic drug delivery systems represents a significant advancement in drug delivery technology, offering improved therapeutic outcomes, patient compliance, and treatment customization. While implantable osmotic pumps with integrated sensors may offer benefits in terms of continuous drug delivery and monitoring, there are concerns about the potential risks associated with implanting electronic devices within the body, such as infection or device malfunction. Additionally, the high cost of these advanced systems may limit accessibility for certain patient populations [22].

ProNeura®

The ProNeura® system provides continuous drug delivery through a small, semi-rigid, and flexible implant composed of a blend of ethylene-vinyl acetate (EVA) and the drug substance. This implant forms a solid matrix, allowing it to be inserted subcutaneously, typically in the inner part of the upper arm, through a straightforward office procedure. At the conclusion of the treatment period, the implant can be easily removed in a similar manner.

Developed to fulfill the demand for a convenient and feasible approach to prolonged drug administration outside of clinical settings, this continuous drug delivery technology offers the potential for uninterrupted therapy lasting six months or more.

Principle of drug release in this technique is takes places by process of dissolution and diffusion through pores in the implant's matrix.

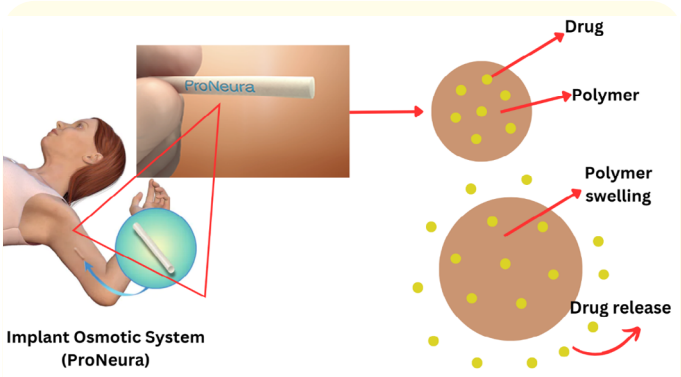

Figure 4: Drug delivery from The ProNeura® system (Implantable osmotic device).

Types of Osmotically Controlled Drug Delivery Systems

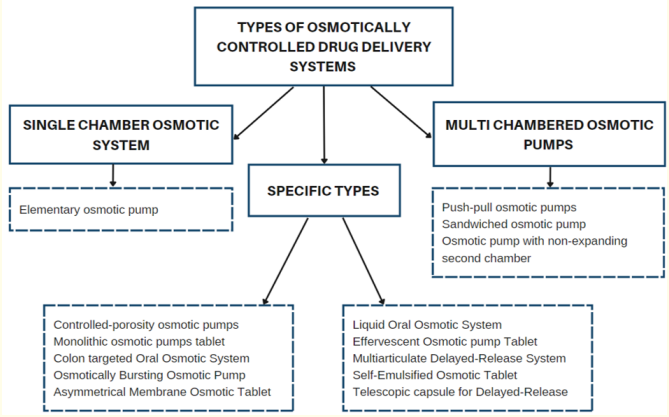

Figure 5: Types of Osmotically Controlled Drug Delivery Systems.

Single chamber osmotic system

Elementary osmotic pump

The elementary osmotic pump, invented by Theuwes in 1974, is a novel drug delivery system employing osmotic processes for controlled release. It operates through the water permeation characteristics of a semipermeable membrane and the osmotic properties of the formulation. This system comprises an osmotically active core surrounded by a semipermeable membrane, often cellulose acetate, with a small drilled hole. The rate of water influx into the core, influenced by membrane permeability and core osmotic pressure, dictates drug release. Initially, the system maintains a constant solute delivery rate until saturation, after which

it declines parabolically towards zero-order release. Despite a lag time of 30-60 minutes for hydration, these devices achieve consistent release of 60-80% of medication, making them suitable for moderately water-soluble drugs. Mechanical and laser drilling are options for membrane perforation, enhancing versatility and precision [23].

Multi chambered osmotic pumps

Push pull osmotic pump (PPOP)

The PPOP, developed by Alza Corporation, features two compartments separated by an elastic diaphragm. A small delivery aperture in the upper compartment allows drug release, while the lower compartment contains a polymeric osmotic agent but lacks a delivery hole. The osmotic polymer constitutes 20-40% of the tablet weight, with the medication layer comprising 60-80%. Upon contact with water, both layers absorb it, causing the diaphragm to expand into the upper chamber, pushing medication through the aperture. Simultaneously, the osmotic agent in the lower compartment attracts water, expanding the non-drug layer and aiding drug expulsion. Carbopol, comprising 20-40% of the tablet, is a common polymer in the push layer. Despite its effectiveness, drawbacks include localized drug distribution and increased cost [24].

Sandwiched osmotic tablets (SOTS)

It consists of two drug layers with two delivery orifices placed between a polymeric push layer. The SOTS can be used for medications that are likely to locally irritate the stomach mucosa because when the tablet is placed in an aqueous environment, the middle push layer, which contains the swelling agent, swells and the drug is released from the two orifices on opposite sides of the tablet [25].

Osmotic pump with non-expanding second chamber

Multi-chamber devices, categorized by the absence of expansion in the second chamber, comprise two subgroups based on their functions. One type dilutes the exiting drug solution to prevent gastrointestinal irritation from saturated solutions. These devices consist of two rigid chambers, the first containing an inert osmotic agent like sugar or sodium chloride, and the second housing the medication. Water ingress through the semi-permeable membrane surrounding the chambers triggers osmosis. The drug solution mixes with the osmotic agent solution from the first chamber before exiting through a microporous membrane. This setup facilitates the delivery of relatively insoluble drugs. These systems offer a controlled release mechanism while mitigating potential irritation from highly concentrated drug solutions, enhancing their suitability for diverse therapeutic applications [26].

Specific types

Controlled porosity osmotic pump

The pump delivery system utilizes either single or multiple compartment dosage forms, each featuring a membrane with an asymmetrical structure consisting of a thin, dense skin layer supported by a porous substructure. The drug-containing core is surrounded by this membrane, created using phase inversion regulated by mixed solvent evaporation. While impermeable to solute, the membrane is permeable to water, facilitated by leaching low concentrations of water-soluble additives from water-permeable, insoluble polymer materials. This results in a controlled porosity, sponge-like structure, enabling controlled release of both water and dissolved pharmacological molecules. Factors such as osmotic pressure difference across the membrane, coating thickness, soluble components in the coating, drug solubility in the core, and water permeability of the semi-permeable membrane influence release rate. However, pH, agitation of release media, and core formulation osmotic pressure do not affect release rate, ensuring robust performance under physiological conditions [27].

Monolithic osmotic system

The monolithic osmotic system is made up of a straightforward dispersion of a water-soluble substance in a matrix of polymer. Polymers have medication particles enclosed within them. The water imbibition by the active agents occurs when the system enters the watery environment, rupturing the polymer matrix capsule containing the medicine and releasing it into the surrounding environment. This process begins in the polymeric matrix's outside environment and gradually moves in a serial fashion into the matrix's interior. These systems control the kinetics of zero-order drug delivery. Osmotic pressure serves as the fundamental energy [28].

Colon targeted oral osmotic system (OROS-CT)

This technique can be used for once- or twice-daily drug formulations that deliver medications specifically to the colon. For targeted colonic medication delivery, the device is coated with 5–6 enteric coating and push–pull osmotic units contained in hard gelatin capsules [26]. When the gelatine capsule shell dissolves after encountering GI fluids, the outer shell of the system inhibits the

passage of fluid from the stomach and it dissolves after entering the intestine. The push compartment and core will enlarge as a result of the water ingestion. The flowable gel is created simultaneously and is pushed out through the delivery hole at a set rate [29].

Osmotically brusting osmotic pump

Baker created a controlled-release delivery device that uses an osmotic bursting process. This system lacks a delivery orifice, and the one that does exist is smaller than the EOP (elementary osmotic system). Water is ingested when it is placed in an aqueous environment, and hydraulic pressure builds up inside the device until the wall ruptures and the contents are expelled into the surrounding area. The semipermeable membrane can regulate medication release by changing its area and thickness. This technique can offer pulsated release, which is helpful [30].

Asymmetrical membrane osmotic tablet

Asymmetric membrane capsules have a core that contains the medicine and are encircled by a membrane with an asymmetric structure, or one that is supported on a thicker, porous part by a comparatively thin, dense section. Unlike a traditional gelatin capsule, which dissolves instantly, an asymmetric membrane capsule allows the active component to be released over a longer period since its wall is comprised of a water-insoluble polymer like cellulose acetate [31].

Liquid oral osmotic system

Liquid OROS systems combine the benefits of prolonged release and high bioavailability, designed for delivering liquid formulations. These systems are particularly suited for controlled release of lipophilic self-emulsifying formulations (SEF). They come in three variations: hard cap L OROS, soft cap L OROS, and systems for delayed liquid bolus delivery. Each system comprises a liquid medication layer, an osmotic engine or push layer, and a semipermeable membrane. Upon contact with water, the rate-controlling membrane allows water ingress, activating the osmotic layer. As the osmotic layer expands, hydrostatic pressure builds up, facilitating delivery of the liquid formulation through the delivery orifice. Developed by Alza, these systems enhance drug permeability, enabling the administration of insoluble medications in aqueous solutions. This approach offers precise control over drug release, ensuring effective and sustained therapeutic outcomes [32].

Effervescent osmotic tablet (EOT)

In this approach, effervescent compounds that react with the acid in the outside environment to produce carbon dioxide are integrated into dosage forms. This gas expands, dispenses the precipitate medication, and stops the aperture from becoming blocked. This system may precipitate at the gastrointestinal pH and block the delivery aperture, making it useful for drugs that are poorly soluble at low pH. In this approach, sodium bicarbonate is typically used [33].

Multiarticulate delayed-release system

In this technique, semipermeable membranes like cellulose acetate are coated on pellets carrying pure medication, with or without an osmotic agent. Water seeps into the system's core and creates a saturated solution of soluble components when it meets the watery environment. A water influx caused by the osmotic pressure gradient causes the membrane to rapidly expand and create pores. Through these holes, the medication and any osmotic ingredients are released in a manner that typically follows zero-order kinetics. The lag time and dissolve rates that rely on the coating thickness and osmotic characteristics of the dissolution media were examined by Schultz and Kleinebudde [34].

Self-emulsified osmotic tablet

Self-emulsifying agents have been added to the tablet-core composition in the case of medications that are just marginally soluble or practically insoluble. The availability of medications with poor aqueous solubility is about 40%. By using a self-emulsifying agent, the self-emulsifying method increases the drug's bioavailability, regulated release rate, and plasma concentration stability. Drugs that are hydrophobic are emulsified. Common surfactants have been utilised for this purpose, including poloxythlenated glyceryl recinoleate, poloxythlenated castor oil with ethylene oxide, glyceryl laureates, and glycerol (sorbiton oleate, stearate, or laurate) [35].

Telescopic capsule for delayed release

This device features two chambers separated by a layer of wax-like material: one for the drug and an exit port, and the other for the osmotic engine. The drug is dispensed into one chamber through a fill mechanism before assembly. A convex osmotic layer and a barrier layer of the bilayer tablet are oriented towards the closed end and the cap opening, respectively. The assembled cap,

osmotic tablet, and vessel are securely fitted together. Upon insertion of the filled vessel into the cap, the osmotic engine expands, exerting pressure on the attached wall portions as fluid is ingested. A slight pressure differential maintains the reservoir volume constant, minimizing net fluid flow into the reservoir during the delay period. This design ensures controlled drug release and efficient fluid management within the dispensing device [36].

Marketed study

There are 31 products on the market that were created and commercialised using the oral osmotic medication method. All these products fall within the therapeutic categories of metabolic diseases (15%), seasonal (25%) and neurological (35%), respectively. Two businesses have created most of these goods; the old Alza Corp., which was later acquired by Johnson and Johnson, created 20 (53%) of them.

Product Name	Company name	Drug substance	Type of osmotic system	Use
UT-15C	United Thera	Treprostinil Diethanolamine	Effervescent Osmotic	Hypertension
LCP-Lerc	Recordati	Lercanidipine	Effervescent Osmotic	Hypertension
Ditropan XL	Johnson and Johnson	Oxybutynin Chloride	Effervescent Osmotic	Overactive bladder
Altoprev	Impax Lab	Lovastatin	Effervescent Osmotic	Hypercholesterolemia
Flexeril XL	Alza Lab	Cyclobenzaprine	Effervescent Osmotic	Muscle relaxant
Elafax XR	Pfizer	Venlafaxine HCl	Effervescent Osmotic	Depression
Tegretol XL	Novartis	Carbamazepine	Effervescent Osmotic	Bipolar disorder
Osmosin	Merck	Indomethacin	Effervescent Osmotic	Pain, fever
Teosona Sol	Johnson and Johnson	Theophylline	Effervescent Osmotic	Asthma
Allegra D 24 h	Phoenix	Pseudoephedrine HCl Fexofenadine HCl	Effervescent Osmotic	Allergic rhinitis
Loremex	Phoenix	Pseudoephedrine HCl Loratadin	Effervescent Osmotic	Allergic rhinitis
Mildugen D	Phoenix	Pseudoephedrine HCl Astemizol	Effervescent Osmotic	Allergic rhinitis
Efidac 24bromphenirmine	Novartis	Pseudoephedrine HCl Brompheniramin	Effervescent Osmotic	Allergic rhinitis
Volmax	GSK	Albuterol	Effervescent Osmotic	Asthma
Acutrim	Carnrick Lab	Phenylpropanolamine	Effervescent Osmotic	Nasal congestion
Teczem	Aventis	Enalapril Diltiazem	Controlled Osmotic Pump	Hypertension
Tiamate	Aventis	Diltiazem HCl	Controlled Osmotic Pump	Hypertension
ActoPlus XR	Andrx	Metformin HCl Pioglitazone HCl	Controlled Osmotic Pump	Diabetes
Covera HS	Upsher-Smith Lab	Verapamil HCl	Push–pull Osmotic	Hypertension
DynaCirc CR	Recordati	Isradipine	Push–pull Osmotic	Hypertension
Minipress XL	Pfizer	Prazosin	Push–pull Osmotic	Hypertension
Procardia XL	Pfizer	Nifedipine	Push–pull Osmotic	Hypertension
Glucotrol XL	Pfizer	Glipizide	Push–pull Osmotic	Hyperglycemia
Cardura CR	Pfizer	Doxazosin Mesylate	Push–pull Osmotic	Hypertension
Oxycontin	Purdue Pharma	Oxycodone	Push–pull Osmotic	Pain relief
Jusnista	Johnson and Johnson	Hydromorphone	Push–pull Osmotic	Pain relief
Invega	Janssen	Paliperidone	Push–pull Osmotic	Bipolar disorder
Topamax	Alza Lab	Topiramate	Push–pull Osmotic	Epilepsy
Concerta	McNeil	Methylphenidate HCl	Push–pull Osmotic	Narcolepsy
ChronogesicTM	Recro Pharma	Sufentanil	Implantable Osmotic	Anesthesia, analgesia
Viadur	Endo Pharma	Leuprolide Acetate	Implantable Osmotic	Cancer

Table 1: Marketed osmosis-based products [37-49].

Conclusion

Osmotic drug delivery systems leverage osmotic pressure to achieve prolonged and regulated drug release, maintaining effective concentrations at the target site over time. This method offers several advantages, including precise control over release profiles, reduced side effects compared to conventional forms, and sustained therapeutic plasma levels. However, challenges such as complex production processes and higher costs limit their widespread application, primarily to chronic conditions like diabetes and hypertension. Recent advancements in osmotic drug delivery systems represent a significant breakthrough, driven by the integration of microchip technology and sensors. These innovations enable remote monitoring of patient adherence and response, personalized therapy optimization, and real-time adjustments based on physiological parameters.

Wireless osmotic drug delivery systems and closed-loop systems offer promising avenues for improving patient outcomes through timely intervention and therapy optimization. Trials of wireless osmotic microchips have shown positive results, although regulatory approval remains pending. Smart osmotic drug delivery devices, exemplified by the LiRIS® device, provide relief for conditions like interstitial cystitis.

Implantable osmotic pumps with sensing capabilities offer continuous drug delivery and monitoring, particularly beneficial for chronic conditions. However, concerns regarding risks and accessibility persist. The ProNeura® system provides a convenient approach for prolonged therapy, utilizing dissolution and diffusion for drug release.

In conclusion, recent advancements in osmotic drug delivery systems hold great promise for enhancing therapeutic outcomes, patient compliance, and treatment customization. While significant progress has been made, challenges such as regulatory approval and accessibility need to be addressed to fully realize the potential of these innovative technologies.

Advantages

- **Higher release rates**: Osmotic systems offer higher release rates compared to traditional diffusion-based methods, ensuring more rapid drug delivery.
- **Independence from hydrodynamic state and pH**: Drug release from osmotic pumps remains unaffected by the body's hydrodynamic state or gastric pH, ensuring consistent performance.
- **Adjustable release control**: The distribution rate of drugs from osmotic devices can be easily adjusted by varying release control settings.
- **Improved patient compliance**: Less frequent dosing due to controlled release leads to better patient compliance with medication regimens.
- **Better release rates**: Osmotic systems achieve superior release rates compared to traditional diffusion methods, enhancing therapeutic efficacy.
- **In vitro-in vivo correlation (IVIVC)**: Within certain limits, there is a significant correlation between in vitro drug release profiles and in vivo performance of osmotic controlled-release drug delivery systems.
- **Enhanced safety**: High-potency medications can be used with osmotic systems, providing a wider margin of safety and reducing adverse effects.
- **Minimal food impact**: Food has minimal impact on the ability of osmotic systems to release drugs, ensuring consistent performance regardless of meal intake.
- **Pause or pulse delivery**: Delivery from osmotic systems can be paused or pulsed as needed, offering flexibility in treatment regimens.
- **Suitable for various drugs**: Osmotic systems are suitable for a wide range of drugs, making them versatile in pharmaceutical applications.
- **Consistent blood levels**: Osmotic systems maintain drug concentrations within the therapeutic range, ensuring consistent therapeutic effects.
- **Clear understanding and formulation**: Osmotic systems are well-defined and comprehended, making formulation and execution simple.
- **Reduced patient variability**: There is less variation in drug response between patients with osmotic drug delivery systems.

Disadvantages

- **Coating process challenges**: The integrity and consistency of the coating process in osmotic systems may pose challenges, leading to film flaws and dose dumping.

- **High investment for laser drilling**: Laser drilling, a common technique for creating delivery orifices in osmotic systems, requires significant investment.
- **Potential allergic reactions**: There is a risk of allergic reactions following implantation of osmotic systems.
- **Inadequate management of coating process**: Poor management of the coating process may result in film flaws and dose dumping, compromising drug release.
- **Importance of hole size**: In simple osmotic systems, the size of delivery orifices is crucial for controlling drug release.
- **Food influence on drug release**: The presence of food may influence drug release from osmotic systems to some extent, affecting therapeutic efficacy.
- **Inability to retrieve therapy**: In the event of an unexpected adverse event, retrieval of therapy from osmotic systems is not possible.
- **Rapid tolerance**: Rapid tolerance development may occur with some drugs delivered via osmotic systems.
- **High cost**: Osmotic drug delivery systems may involve high initial costs, limiting accessibility for some patients.

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