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An Osmotic Drug Delivery System as a Component of a Modified Release Dosage Form- A comprehensive review.

Shwetanjali Sabaji Naikodi

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ABSTRACT: Novel drug delivery systems (NDDS) like osmotic pumps have gained attention in food and pharmaceutical industries for controlled drug delivery in humans and animals. These pumps are operated by osmotic pressure, which releases active compounds. Drug release from such a mechanism is largely gastro-fluid-independent. Drugs are known to be released immediately by conventional drug delivery systems, making it impossible to control the release of the drug and to keep an effective concentration at the target site for an extended period. Drug release can be spatially controlled with the use of controlled drug delivery systems. The most promising technologies for regulated drug administration are osmotic pumps. Both oral delivery and implantable utilize these technologies. The Rose-Nelson pump, the Higuchi-Leeper pumps, the Alzet and Osmet systems, the basic osmotic pump, and the push-pull system were all developed as a part of the osmotic system history. Recent developments include the creation of the controlled porosity osmotic pump and asymmetric membrane-based devices. Osmotic pumps have an inner core that is coated in a semipermeable membrane and contains a drug and osmogens. The drug solution is forced out through the delivery ports as the core's volume increases as a result of the absorption of water. The drug is released by osmotic pumps at a rate that is unaffected by the hydrodynamics and pH of the dissolution medium. This review summarizes the available osmotic devices for implantation and osmotic tablets for oral administration.

KEYWORDS: Osmosis, Osmotic pressure, Osmotic drug delivery system, semi-permeable membrane, controlled release system, novel drug delivery system.

I. INTRODUCTION

During the past three decades, significant advances have been made in the area of novel drug delivery. The reason for this development is the relatively low development cost and time required for introducing an NDDS ($20–50 million and 3–4 years, respectively) as compared to a new chemical entity (approximately $500 million and 10–12 years, respectively).1 In the form of NDDS, an existing drug molecule can get a ‘new life,’ thereby, increasing its market value, competitiveness, and patent life. Several design options are available to control or modulate the drug release from a dosage form.

The majority of oral dosage forms fall in the matrix, reservoir, or osmotic system category. In a matrix system, the drug is embedded in the polymer matrix and the release takes place by partitioning of drug into the polymer matrix and the release medium. In contrast, reservoir systems have a drug core surrounded and coated by the rate-controlling membrane. However, factors like pH, the presence of food, and another physiological factor may affect drug release from conventional controlled release systems. Osmotic systems utilize the principle of osmotic pressure for the delivery of drugs. Drug release from these systems is largely independent of pH and other physiological parameters, and it is possible to modulate the release characteristic by optimizing the properties of the drug and system. Using osmotic pressure as the energy source, the semi-permeable membrane controls water inflow, generating hydrodynamic pressure inside the device and, thereby controlling drug delivery.

Osmotic delivery systems or osmotic pumps are mainly composed of a core containing a drug and an osmogen. These are coated with a semi-permeable membrane containing one or more ports for drug delivery, such that the drug is released over time in the form of a solution or suspension. Oral osmotic systems are composed of a compressed tablet core coated with a semi-permeable membrane through which delivery orifices are created using a laser beam or mechanical drill. These controlled systems are based on osmosis and osmotic pressure and are independent of various gastrointestinal factors. However, it is noteworthy that there are critical factors that influence the design of osmotically controlled drug delivery systems,

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including the drug solubility, delivery orifices, osmotic pressure, semi-permeable membrane, type and nature of the polymer, membrane thickness, and type and amount of plasticizer[1].

1.1. Advantages of Osmotically Controlled Drug Delivery System[2,3]:

1. They typically give a zero-order release profile after an initial lag.
2. Deliveries may be delayed or pulsed if desired.
3. Drug release is independent of gastric pH and hydrodynamic condition.
4. They are well characterized and understood.
5. The release mechanisms are not dependent on drugs.
6. A high degree of in-vitro and in-vivo correlation (ivivc) is obtained in osmotic systems.
7. The rationale for this approach is that the presence of water in it is relatively constant, at least in terms of the amount required for activation and controlling osmotically base technologies.
8. Higher release rates are possible with osmotic systems compared with conventional diffusion-controlled drug delivery systems.
9. The release from osmotic systems is minimally affected by the presence of food in the gastrointestinal tract.
10. The release rate of osmotic systems is highly predictable and can be programmed by modulating the release control parameters.

1.2. Disadvantages of Osmotically Controlled Drug Delivery System:

1. Expensive
2. If the coating process is not well controlled there is a risk of film defects, which results in dose dumping
3. Size hole is critical
4. Dose dumping
5. Retrieval therapy is not possible in the case of unexpected adverse events.

2. Basic Components of Osmotic Pump Systems

2.1. Drug

Not every drug administered needs to provide a prolonged response, so the osmotic pump system is not suitable for all drugs. Drugs that are indicated for the prolonged treatment of diseases with a biological half-life in the range of 1–6 h are best suited for osmotic systems. Drugs with a biological half-life shorter than 1 h are not good candidates, and, similarly, drugs with a half-life greater than 12 h are also not good candidates for controlled release in an osmotic pump system. The drug's half-life should be short so that it can be sustained or maintained in plasma, and its prolonged release should be the requirement[4]. To be incorporated into this system, drugs should also be neither highly soluble nor very poorly soluble, and the nature of the drug should be potent for this purpose[5,6].

2.2. Osmotic Agent

Osmogens and osmogents are other names for osmotic agents, and they create osmotic pressure in the osmotic delivery system. When a drug has low solubility, it will be released at a slow, first-order rate; to make this release rate faster, osmotic agents are used in the formulation. These agents generate a high gradient of osmotic pressure within the osmotic system; thus, the rate of drug release increases[7]. The osmotic agents available on the market include lactose, fructose, sorbitol, dextrose, sodium chloride, citric acid, potassium chloride, sucrose, xylitol, and mannitol. Osmogens may also consist of mixtures, such as mannitol + sucrose, dextrose + fructose, sucrose + fructose, dextrose + sucrose, mannitol + fructose, lactose + fructose, mannitol + dextrose, or lactose + dextrose[8]. Drugs with good water solubility can be used as osmotic agents, such as mannitol, glycerol, lactulose, sorbitol, or polyethylene glycol. However, osmogenic salts (e.g., sodium chloride and potassium chloride) and sugars can be incorporated into the formulation if the drug itself does not possess osmogenic activity. Hence, water solubility and osmotic activity are the two most important determinant factors when selecting osmotic agents[9].

2.3. Semipermeable Membrane

As the nature of the osmotic system membrane is selectively permeable, the polymer should be selectively permeable, to allow for the passage of water only, and should be impermeable to solutes[10]. In osmotic pump preparation, the polymer that is most commonly and extensively used is cellulose acetate, which is provided in various grades of acetyl content[11]. The grades containing 32% and 38% acetyl content are most commonly employed. The degree of substitution (average no. of hydroxyl groups replaced by substituting groups) determines the acetyl content. Other digestive polymers used for this purpose include cellulose esters, like diacetate, propionate, cellulose acetate, triacetate, and cellulose acetate butyrate. Ethers of cellulose can also be included in this, such as ethyl cellulose[12,13]. The material must have sufficient wet strength to retain the integrity of

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its dimensions, which is beneficial for the device. The ability of the material to allow water permeation must be sufficient so that the flux rate of water stays within the required range. The transmission rates of water vapor can be calculated to estimate the water flux rates. The biocompatibility of the membrane material should also be considered[14]. Common biocompatible polymers include PEG, HPMA, PGA, chitosan, and dextran. These materials, when used in oral systems, can be ingested and then excreted in feces once the osmotic pump is exhausted. Oral and implant fractions that may have been absorbed are very likely to be eliminated by glomerular filtration in the kidney, provided that they are below the glomerular threshold[15].

2.4. Wicking Agent[16]

Wicking agents are substances with the ability to absorb water into the porous network of a delivery system. Their main function is to carry solvent molecules to surfaces inside the core of the osmotic device, thereby creating channels of enhanced surface area. A wicking agent is selected based on its nature, either swellable or non-swellable, and based on its ability to undergo physisorption with solvent molecules. Physisorption is a form of Vander Waals interaction where the solvent molecules can loosely adhere to the surface of the wicking agent[17]. Sodium lauryl sulphate, polyvinylpyrrolidone, and colloidal silicon dioxide are examples of such agents[18].

2.5. Pore-Forming Agents

A microporous membrane forms due to the presence of pore-forming agents. A pore former can also form walls with micro-sized pores. This pore former leaches out, creating pores as the system operates[19]. Alkaline metal salts such as potassium chloride, sodium chloride, and others may be used as pore-forming agents. Alkaline earth metals such as calcium nitrate and carbohydrates such as fructose and glucose can also be employed for this purpose[20].

2.6. Coating Solvents

The solvent system conveys the polymer, which is dispersed or dissolved, and other additives to the substrate surface as its primary function. Solvents that are inert and either organic or inorganic in nature are employed to prepare a polymeric solution[21]. These solvents should not cause adverse actions in the core or other materials. Examples of such solvents include methanol, cyclohexane, methylene chloride, isopropyl alcohol, and water[22].

2.7. Surfactants

Surfactants are particularly useful when added to wall-forming material. They produce an integral composite that is useful for making the wall of the device operative. The surfactants act by regulating the surface energy of materials to improve their blending into the composite and maintain their integrity in the environment of use during the drug release period. Typical surfactants such as poly oxyethylenated glyceryl recinoleate, polyoxyethylenated castor oil having ethylene oxide, glyceryl laurates, and glycerol (sorbitan oleate, stearate, or laurate) are incorporated into the formulation.

2.8. Plasticizers

In pharmaceutical coatings, plasticizers, or low molecular weight diluents are added to modify the physical properties and improve the film-forming characteristics of polymers. Plasticizers can change the viscoelasticbehavior of polymers significantly[23]. Plasticizers can turn a hard and brittle polymer into a softer, more pliable material, and possibly make it more resistant to mechanical stress[24]. Plasticizers lower the temperature of the second-order-phase transition of the wall or the elastic modulus of the wall and also increase the workability, flexibility, and permeability of the coating solvents. Generally, from 0.001 to 50 parts of a plasticizer or a mixture of plasticizers are incorporated into 100 parts of costing materials. PEG-600, PEG-200, triacetin (TA), dibutyl sebacate, ethylene glycol monoacetate, ethylene glycol diacetate, triethyl phosphate, and diethyl tartrate are used as plasticizers in the formulation of semipermeable membrane[25,26].

3.Delivery orifice

The drug is delivered through an orifice via the process of diffusion to achieve an optimal, zero-order rug delivery rate[27]. The cross-sectional area of the orifice must be small, but it should not be too small to create hydrostatic pressure in the osmotic system. This means that the orifice must be larger than the minimum size requirement. The optimum size range for a delivery orifice is 600 µm to 1 mm[28,29]. The delivery orifice can be created via a simple mechanical drilling method[30]. Another technique used to create orifices in the sub-millimeter range is laser drilling technology. The laser beam generally used for this purpose is CO_2, and it has proved to be beneficial and

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economical[31,32]. Leaching materials can also be employed for creating in situ orifices or pores in the membrane[33]. There is a process known as indentation in core tablets that utilizes updated compression punches. The upper punch contains needles for the creation of orifices[34].

4. Types of Osmotically Controlled Drug Delivery System[35]:

Many forms of osmotic pumps are reported in the literature but, in general, they can be divided into oral and implantable systems.

4.1. Osmotic Implantable Formulation System

4.1.1. The Rose and Nelson Pump
4.1.2. Higuchi Leeper Pump
4.1.3. Higuchi Theuwes pump

4.2. Osmotic Oral Formulation System

4.2.1. Elementary Osmotic Pump (EOP)
4.2.2. Push Pull Osmotic Pump
4.2.3. Osmotic Bursting Osmotic Pump
4.2.4. Liquid Oral Osmotic System
4.2.5. Sandwiched Osmotic Tablets (SOTS)
4.2.6. Delayed Delivery Osmotic Device
4.2.7. Monolithic Osmotic System
4.2.8. Controlled Porosity Osmotic Pump
4.2.9. Telescopic Capsules
4.2.10. OROS-CT
4.2.11. Osmat

4.1. Implantable Systems

4.1.1. The Rose–Nelson Pump

The first implantable osmotic technique pump was reported in 1955 by Rose and Nelson, Australian physiologists. The pump was designed to deliver drugs into the guts of animals (sheep and cattle)[36]. A semi-permeable wall and water chamber surround an elastic diaphragm consisting of a section of excess salt. These two chambers are separated by a semi-permeable barrier. This creates a difference in gradient and osmotic pressure; thus, the water tends to move towards the chamber of salt from its chamber. As water enters the salt chamber, the volume of the salt chamber increases; hence, the diaphragm starts to distend, resulting in the pumping of the drug. The drug is then pumped out of the device[37](Figure no. 1).

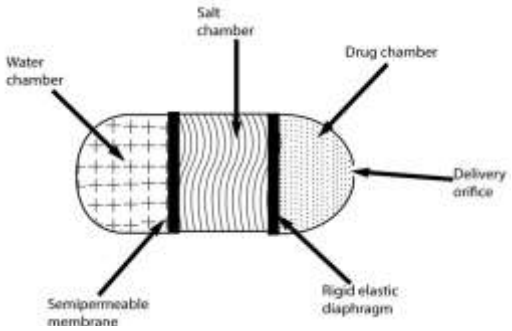

Figure no. 1

4.1.2. The Higuchi–Leeper Pump

In the 1970s, Alza Corporation introduced the Higuchi–Leeper pump (Figure 2), a simplified form of the Rose–Nelson pump[38]. The water chamber is absent in the Higuchi–Leeper pump. Instead, the water required for device activation is drawn from the environment in the device's surrounding[39]. This is a beneficial modification, as it enables the storage of prepared and drug-loaded pumps for a month[40].

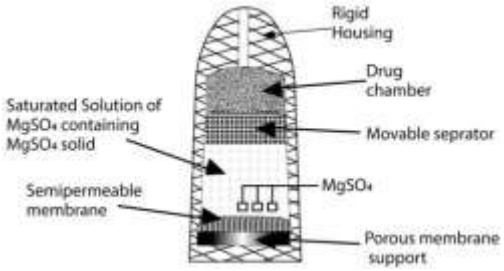

Figure no. 2

4.1.3. The Higuchi–Theeuwes Pump

In the 1970s, Higuchi and Theeuwes introduced a pump that had an outer casing made up of a rigid semi-permeable membrane (Figure 3). This pump is similar in form to the Rose–Nelson pump. The drug is loaded into the device before use[41]. The rate of drug release from the device when it is operated depends on the outer membrane's permeation ability, and a time course that the salt has set is followed[42].

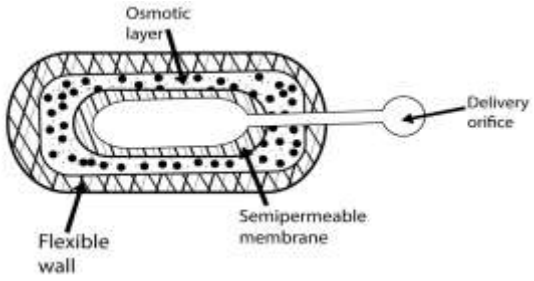

Figure no. 3

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4.2. Oral Systems

4.2.1. Elementary Osmotic Pump (EOP)

An EOP is a new system for drug delivery by an osmotic system invented by Theuwes in 1974. The release rate can be controlled by controlling the permeation ability of the semi-permeable membrane and the formulation characteristics[43]. In the formation of this device, the drug is compressed into a tablet, and then a coating of a semi-permeable cellulose acetate membrane is formed around it[44]. An orifice of about 0.5 to 1.5 mm is drilled into this membrane (Figure 4). A mechanical drill can be used for this purpose, but it can also be carried out by laser drilling using a CO_2 laser beam with a 10.6-micron wavelength. When the device is put into operation, water enters through a semi-permeable wall by imbibition into the core, creating osmotic pressure. The drug solution volume is proportional to the solvent volume[45]. The rate of drug release is zero-order, which means that it is constant. The development of zero-order rates from the system requires a half-hour to one-hour lag phase before continuous delivery begins. About 60–80% of the drug has a constant drug release rate. Drugs with moderate water solubility are considered suitable for this system[46].

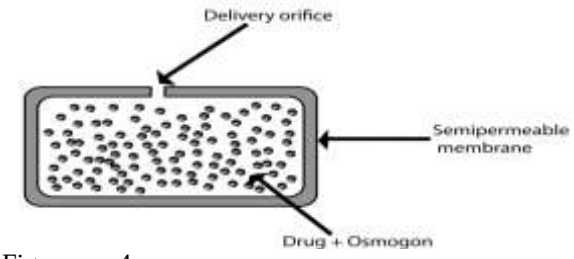

Figure no. 4

4.2.2. Push Pull Osmotic Pump

Push-pull osmotic systems (PPOS), also known as push-pull osmotic pumps, have been successfully developed and marketed to extend the release of poorly soluble compounds for various indications, such as hypertension, diabetes, and asthma. In these chronic disease treatments, PPOS was reported as a drug delivery technology reducing the food interaction often observed with poorly soluble drug substances as well as enabling a once-a-day administration and thereby patient compliance. Push Pull Osmotic Pump is possible to deliver both poorly water-soluble and highly water-soluble drugs at a constant rate[47]. One layer (depict as the upper layer) contains the drugs in a formulation of polymeric, osmotic agents, and other tablet excipients. This polymeric osmotic agent can form a suspension of the drug in situ. When this tablet later imbibes water, the other layer contains osmotic and coloring agents, polymer, and tablet excipients. These layers are formed and bonded together by tablet compression to form a single bilayer core. The tablet core is then coated with a semi-permeable membrane. After the coating has been applied, a small hole is drilled through the membrane by a laser or mechanical drill on the drug layer side of the tablet. When the system is placed in aqueous environment water is attracted into the tablet by an osmotic agent in both the layers as shown in figure number 5. The osmotic attraction in the drug layer pulls water into the compartment to form in situ a suspension of the drug. The osmotic agent in the non-drug layer simultaneously attracts water into that compartment, causing it to expand volumetrically and the expansion of the non-drug layer pushes the drug suspension out of the delivery orifice.

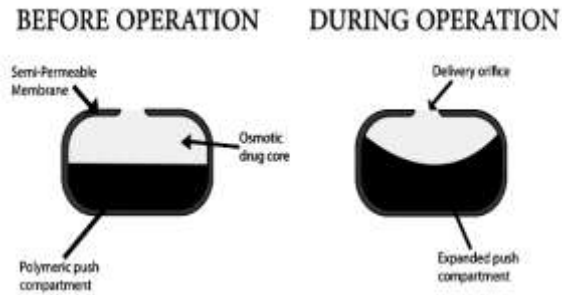

Figure no. 5

4.2.3. Osmotically Bursting Osmotic Pump

Baker invented this system of controlling drug release. The orifice for drug delivery may either be absent in this system or present at a very small size[48]. When water enters the system in the aqueous environment, hydraulic pressure forms. This ruptures the system, releasing its contents into the surroundings. The pulsatile release can be achieved when using this system. By controlling the thickness and area of the semi-permeable membrane, the drug release rate can be controlled in this system[49].

4.2.4. Liquid Oral Osmotic System

Liquid forms of drugs are delivered via this design, providing a high rate and extent of absorption and giving the advantage of extended release. A liquid drug formulation that is self-emulsifying and lipophilic is considered desirable for this system[50]. A semi-permeable membrane encloses an osmotic push layer. A drug layer represents the structure of this design, which is available in three forms (hard cap, soft cap, and

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delayed liquid bolus)[51]. Water imbibition activates the osmotic agent layer on exposure to an aqueous environment. This expands the push layer, and hydrostatic pressure pushes the drug out of the device system. Alza design these systems. This system increases the permeation ability of drugs[52].

4.2.5. Sandwiched Osmotic Tablets (SOTS)

It is composed of a polymeric push layer sandwiched between two drug layers with two delivery orifices. When placed in the aqueous environment the middle push layer containing the swelling agents swells and the drug is released from the two orifices situated on opposite sides of the tablet as shown in Figure number 6 thus SOTS can be suitable for drugs prone to cause local irritation of the gastric mucosa[53].

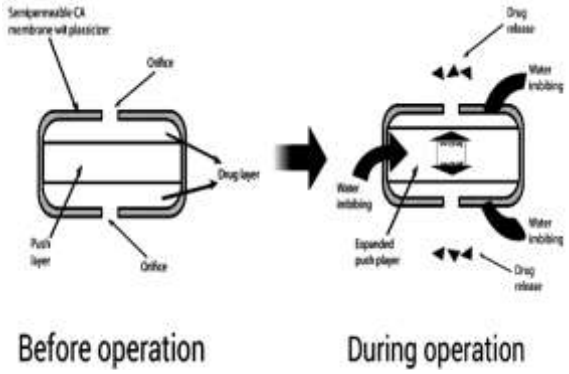

Figure no. 6

4.2.6. Delayed Delivery Osmotic Device

This device consists of two chambers, the first contains the drug and an exit port, and the second contains an osmotic engine. A layer of wax-like material separates the two sections. To assemble the delivery device, the desired active agent is placed into one of the sections by manual or automated fill mechanism. The bilayer tablet with the osmotic engine is placed into a completed cap part of the capsule with the convex osmotic layer pointed into the closed end of the cap and the barrier into the closed end of the cap and the barrier layer exposed towards the cap opening. The open end of the filled vessel is fitted inside the open end of the cap, and the two pieces are compressed together until the cap, osmotic bilayer tablet, and vessel fit together tightly. As fluid is imbibed in the housing of the dispensing device, the osmotic engine expands and exerts pressure on the slidable connected first and second wall sections. During the delay period, the volume of a reservoir containing the active agent is kept constant, therefore a negligible pressure gradient exists between the environment of use and the interior of the reservoir. As a result, the net flow of environmental fluid driven by the pressure entering the reservoir is minimal, and consequently, no agent is delivered for the period[54].

4.2.7. Monolithic Osmotic System

This system includes agents that are soluble in water and are dispersed in a matrix of polymers [55]. Polymers form the capsule around the drug. Upon contact with aqueous surroundings, the active ingredients draw water into the system, resulting in the rupture of the polymeric capsule around the drug, thus releasing the drug out of the system[56]. These phenomena move serially from the outer material side toward the inner side of the polymer matrix. The release is driven by osmotic pressure at a zero-order rate[57,58].

4.2.8. Controlled Porosity Osmotic Pump

This osmotic pump tablet consists of a core compartment loaded with drugs with some water-soluble additives coated by an asymmetric insoluble membrane (Figure 7). The membrane has selective permeability for water only[59]. When exposed to the aqueous environment, water-soluble additives start dissolving and leaching out of the system, resulting in the formation of micropores in the membrane, giving it a spongelike appearance. The microporous wall formed is then permeable to water and the drug in dissolved form. Sorbitol, urea, and sodium chloride are some of the pore-formers used[60]. Materials that can produce 5–95% pores and pore sizes in the range of 10–100 µm are beneficial. Different studies have been conducted to study the mechanism of drug release with moderate to high solubility, and some modulators of solubility are also being studied[61]. The thickness of the soluble portion and drug solubility, osmotic pressure, and coating surface area are the factors that affect the drug release rate from this system. However, this system does not depend on pH or physiological conditions. The designer of the device can control all of these factors[62].

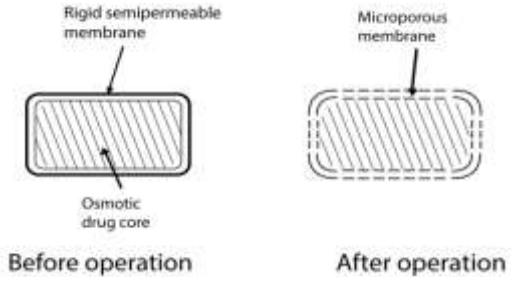

Figure no. 7

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4.2.9. Telescopic Capsules

This system consists of a waxy layer separating two chambers. The drug is contained in the first chamber with an orifice, while an osmotic agent is present in the second chamber. An automated mechanism fills the drug. The capsule cap contains a bilayer tablet, while the cap's closed end includes a barrier (Figure 8). The capsule's open end is fitted with a filled vessel. Compression is applied to this assembly[63,64]. When water enters the system, the expansion of the osmotic layer occurs, resulting in pressure generation on the wall of sections. The drug volume is constant in the delay period to minimize the fluid's net flow into the core of the system[20].

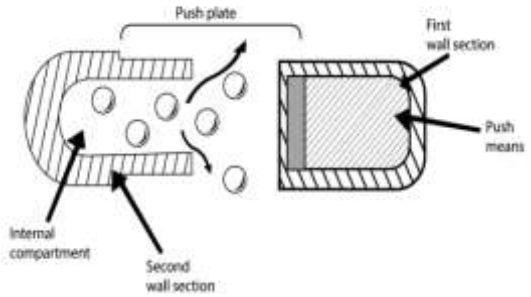

Figure no. 8

4.2.10. OROS-CT

OROS-CT is used as a once or twice-a-day formulation for targeted delivery of drugs to the colon. The OROS-CT can be a single osmotic agent or it can be comprised of as many as five to six push-pull osmotic units filled in a hard gelatine capsule. After coming in contact with the gastric fluids, the gelatine capsule dissolved and the enteric coating prevents entry of fluids from the stomach to the system as the system enters into the small intestine the enteric coating dissolves and water is imbibed into the core thereby causing the push compartment to swell. At the same time, flowable gel is formed in the drug compartment, which is pushed out of the orifice at a rate, which is precisely controlled, by the rate of water transport across the semi-permeable membrane[65].

4.2.11. Osmat

It is a novel osmotically driven matrix system, which utilizes the hydrophilic polymers to swell, and gel in an aqueous medium forming a semi-permeable membrane in-situ releases from such a matrix system containing an osmogen could, therefore be modulated by the osmotic phenomenon. Osmat thus judiciously combines both matrix osmotic characteristics resulting in a quantum improvement in drug delivery from a swellable matrix system. Osmat produces controlled drug release with adequate delivery rates in agitation in a dependent manner. Thus, osmat represents a simple, versatile, and easy-to-fabricate osmotically driven controlled drug delivery system based upon low-cost technology[66].

5. Factors Affecting Drug Release Rate

5.1. Drug Solubility
5.2. Osmotic Pressure
5.3. Delivery Orifice
5.4. Coating Membrane

5.1. Drug Solubility

APIs for osmotic delivery should have water solubility in the desired range to get optimize drug release. However, by modulating the solubility of these drugs within the core, effective release patterns may be obtained for the drugs, which might otherwise appear to be poor candidates for osmotic delivery.

Solubility-modifying approaches:

- Use of swellable polymers: vinyl acetate copolymer, and polyethylene oxide has a uniform swelling rate which causes drug release at a constant rate.
- Use of wicking agents: These agents may enhance the surface area of the drug with the incoming aqueous fluids. e.g., colloidal silicon dioxide, sodium lauryl sulphate, etc. Ensotrol® technology uses the same principle to deliver drugs via the osmotic mechanism.
- Use of effervescent mixture: A mixture of citric acid and sodium bicarbonate creates pressures in the osmotic system and ultimately controls the release rate.
- Use of cyclodextrin derivatives: They are known to increase the solubility of poorly soluble drugs. The same phenomenon can also be used for the osmotic systems.
- Use of alternative salt form: Change in salt form may change solubility.
- Use of encapsulated excipients: Solubility modifier excipient used in the form of mini-tablet coated with rate-controlling membrane.
- Resin Modulation approach: Ion-exchange resin methods are commonly used to modify the solubility of APIs. Some of the resins used in osmotic systems are Poly (4-vinyl pyridine), Pentaerythritol, citric and adipic acids.
- Use of crystal habit modifiers: Different crystal forms of the drug may have different solubility,

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so the excipient which may change the crystal habit of the drug can be used to modulate solubility.

- Co-compression of drug with excipients: Different excipients can be used to modulate the solubility of APIs with different mechanisms like saturation solubility, and pH-dependent solubility. Examples of such excipients are organic acids, buffering agents, etc.

5.2. Osmotic Pressure

The next release-controlling factor that must be optimized is the osmotic pressure gradient between inside the compartment and the external environment. The simplest and most predictable way to achieve a constant osmotic pressure is to maintain a saturated solution of the osmotic agent in the compartment.

5.3. Delivery Orifice

To achieve an optimal zero-order delivery profile, the cross-sectional area of the orifice must be smaller than the maximum size to minimize drug delivery by diffusion through the orifice. Furthermore, the area must be sufficiently large, above a minimum size to minimize hydrostatic pressure build-up in the system. The typical orifice size in osmotic pumps ranges from 600µ to 1 mm. Methods to create a delivery orifice in the osmotic tablet coating are:

- Mechanical drill
- Laser drill: This technology is well established for producing sub-millimeter size holes in tablets. Normally, CO2 laser beam (with an output wavelength of 10.6µ) is used for drilling purposes, which offers excellent reliability characteristics at low costs.
- Indentation that is not covered during the coating process: Indentation is made in core tablets by using modified punches having a needle on the upper punch. This indentation is not covered during the coating process which acts as a path for drug release in the osmotic system.
- Use of leachable substances in the semi-permeable coating: e.g., controlled porosity osmotic pump.

5.4. Coating Membrane

The thickness of the membrane has a profound effect on the drug release from osmotic systems. The release rate from osmotic systems is inversely proportional to the membrane thickness. The thickness can be controlled by altering the permeability of coating polymer with different pharmaceutical plasticizers such as PEG-200, PEG-600, dibutyl sebacate, triethyl phosphate, diethyl tartrate, diacetin, and ethylene glycol.

6. Evaluation Parameter of Osmotic Drug Delivery Formulation

- Characterization of dosage form
- Effect of osmotic agents
- Swelling properties
- Membrane stability and thickness
- Orifice diameter and drug release
- In-vitro drug release study

Product name	Active pharmaceutical ingredient	Design of osmotic pump
Acutrim	Phenylpropanolamine	Elementary pump osmotic pump
Alpress LP	Prazosin	Push-pull osmotic pump
Cardura XL	Doxazosin	Push-pull osmotic pump
ChronogesicTM	Sufentanil	Implantable osmotic system
Covera HS	Verapamil	Push-pull osmotic pump
Ditropan XL	Oxybutynin chloride	Push-pull osmotic pump
Dynacirc CR	Isradipine	Push-pull osmotic pump

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UT-15C	Treprostinil Diethanolamine	Elementary pump osmotic pump
LCP-Lerc	Lercanidipine	Elementary pump osmotic pump
Ditropan XL	Oxybutynin Chloride	Elementary pump osmotic pump
Altoprev	Lovastatin	Elementary pump osmotic pump
Flexeril XL	Cyclobenzaprine	Elementary pump osmotic pump
Elafax XR	Venlafaxine HCl	Elementary pump osmotic pump
Tegretol XL	Carbamazepine	Elementary pump osmotic pump
Osmosin	Indomethacin	Elementary pump osmotic pump
Teosona Sol	Theophylline	Elementary pump osmotic pump
Allegra D 24 h	Pseudoephedrine HCl Fexofenadine HCl	Elementary pump osmotic pump
Loremex	Pseudoephedrine HCl Loratadin	Elementary pump osmotic pump
Mildugen D	Pseudoephedrine HCl Astemizol	Elementary pump osmotic pump
Efidac 24bromph enirmine	Pseudoephedrine HCl Brompheniramin	Elementary pump osmotic pump
Volmax	Albuterol	Elementary pump osmotic pump
Osmoran	Ranitidine HCl	Elementary pump osmotic pump
Teczem	Enalapril Diltiazem	Push-pull Osmotic Pump
Tiamate	Diltiazem HCl	Push-pull Osmotic Pump
ActoPlus XR	Metformin HCl Pioglitazone HCl	Push–pull Osmotic Pump
Acu System C	Vitamin C	Push-pull Osmotic Pump
Minipress XL	Prazosin	Push–pull Osmotic Pump
Procardia XL	Nifedipine	Push–pull Osmotic Pump
Glucotrol XL	Glipizide	Push–pull Osmotic Pump

II. CONCLUSION

One of the technologies for controlled drug delivery is the osmotic pump. Osmogen is often found in a drug core that is coated with a semipermeable membrane in osmotic drug delivery systems. One or more delivery ports in this coating allow the medicine to be released over time as a solution or suspension. Various osmotic systems include the Rose-Nelson pump, the Higuchi-Leeper pump, the elementary osmotic pump, and the push-pull pump. Recent advances include the development of the controlled porosity osmotic

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pump, L-OROS pump, and sandwiched osmotic tablet. In the future, various attempts are made to produce successful osmotic systems like pulsatile delivery based on an expandable orifice, lipid osmotic pump, telescopic capsule containing mini osmotic pump for delayed release, osmotic bursting osmotic pump, and so forth. The main clinical advantages of this method come from its ability to deliver a drug at a set rate independent of physiological factors like food intake or patient age. Osmotic pumps are in a class by themselves among the numerous drug delivery methods due to their distinct benefits over other dosage forms, and several products based on this technology are on the market. Despite the controversy concerning the safety in the administration of non-disintegrable tablets, the reported clinical benefits have opened up new perspectives to the future development of drugs as oral osmotically driven systems.

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