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A Comprehensive Review on Osmotic Controlled Drug Delivery System.

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ABSTRACT

The conventional drug delivery systems provide an immediate release of the drug in which the release of the drug cannot be managed and the effective concentration at the target site cannot be sustained for a longer time. This form of dosage pattern can lead to plasma concentration fluctuation. Osmotic systems are the most effective strategy-based drug delivery control system. They work on the osmotic pressure principle to control the drug's delivery. The release of the drug is largely independent of the GIT's physiological factors. Such processes use osmosis as the main driving force for the release of drugs. For the osmotic drug delivery system, adequate water solubility of the drug is necessary. Osmotic drug delivery systems are composed of a drug core that is osmotically active and surrounded by a semi-permeable membrane. Numerous formulation factors such as osmotic pressure of the core component(s), solubility and size of the delivery orifice, and the nature of semi-permeable membrane influence drug(s) release from osmotic systems. This review offers a brief description of components, ideal drug characteristics, types of osmotically regulated pump and its mechanism, advantages, disadvantages.

Keywords: Osmotic drug delivery, Sandwiched Osmotic system, Osmotic pump, Osmotic pressure.

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INTRODUCTION

Oral drug delivery is the most favored and convenient option since the oral route offers maximum active surface area for the administration of various drugs among all drug delivery systems.¹ There is little or no control over the release of the drug in conventional oral drug delivery systems and successful concentration can be achieved at the target site through the irregular administration of excessive dose. The consequence of this form of dosage pattern results in fluctuation of concentrations of therapeutic plasma, contributing to some significant side effects. In addition, the rate and degree of drug absorption from conventional dosage forms can vary greatly depending on factors such as excipient presence, physicochemical properties of the medication, various physiological factors such as the presence or absence of food, pH of the GIT tract, gastrointestinal motility, etc. Local gastrointestinal or systemic toxicity can be caused by uncontrolled rapid release of the drug. Therefore, different approaches are taken in the design of formulations that will overcome the disadvantages of conventional dosage forms, including a sustained/controlled system of drug delivery. There are three major groups of drug delivery controlled; trans-dermal, intravenous and oral route.² Oral osmotic controlled release (CR) delivery systems uses osmotic pressure to control active agent distribution.³ Substance release from these systems is largely independent of pH and other physiological parameters and by modifying the properties of substance and system it is possible to modulate the release characteristics.² The first to create an oral osmotic pump was the U.S. Alza Corporation R.

History of osmotic drug delivery system:⁴

About 75 years after the discovery of the principle of osmosis, the drug delivery systems were clearly designed. The Australian scientists Rose and Nelson were initiators of the delivery of osmotic drugs. In 1955 an implantable pump was developed, consisting of three chambers: a drug chamber, a salt chamber containing excess solid salt, and a water chamber. In 1975-the introduction of the elementary osmotic pump for oral drug delivery. The pump is a drug-containing osmotic core surrounded by a semi-permeable membrane with a delivery orifice. When this pump is exposed to water, the core osmotically absorbs water at a regulated rate, defined by the water permeability of the membrane and the core formulation osmotic pressure. Since the membrane cannot be expanded, the increase in volume caused by water imbibition leads to the development of hydrostatic pressure within the tablet. This pressure is eased through the delivery orifice by the flow of saturated solution out of the device. In the 1970s, implantable osmotic pumps were a major

breakthrough in the delivery of a wide range of drugs and hormones, including constantly programmed peptides.

Advantages of Osmotic Drug Delivery System:^{5,6}

In addition to the overall advantages of controlled drug delivery systems, osmotic pumps have some unique advantages as follows:

1. Drug delivery from osmotic pumps can be configured to obey the true kinetics of zero-order.
2. Delivery, if needed, can be delayed or pulsed.
3. Drug release is independent of the body's gastric pH and hydrodynamic conditions from osmotic pumps.
4. Higher release rates from osmotic systems are possible than with conventional drug delivery systems based on diffusion.
5. By modulating the release control parameters, the delivery rate of drugs from these systems is highly predictable and programmable
6. It is possible to obtain a high degree of differentiation between In vitro and In vivo from osmotic pumps.
7. The quality of food is minimally impaired by the release of drugs from osmotic processes.

Disadvantages Of Osmotic Drug Delivery System:^{7,8}

1. Cannot crush or chew products: Osmotic pump tablet should not be crushed or chewed as it may result in loss of the characteristics of 'slow release' as well as toxicity.
2. Release rate: Nutrition and gastric transit time may affect the rate of release of drugs; as a result, variations in the rate of release between doses can occur.

Limitations:⁹

Across different clinical fields, Osmotic Drug Delivery Systems has provided significant benefits. Many systems have increased patient compliance, while others have reduced their active compound's side effects. Nevertheless, there have been studies of some drawbacks of osmotic drug delivery systems.

1. Slightly higher cost than the ion capsule form of the matrix tablet or multi-particle capsule.
2. Cases of gastrointestinal obstruction with the patient receiving Nifedipine tablet have been reported.
3. Other cases of osmosin (Indomethacin OROS) have been reported as frequent occurrences of severe gastrointestinal reaction leading to the withdrawal of osmosin.

4. If the coating process is not well regulated, there is a chance of film defects resulting in dose dumping.
5. Size hole is critical.
6. In case of unforeseen adverse events, retrial therapy is not feasible.

Formulation of Osmotic Drug Delivery System:^{10,11}

Drugs:

Characteristics of drug candidate for osmotically controlled drug delivery.

- It is supposed to have short half-life (2-4 hours).
- It is necessary to desire prolonged release of the drug.
- In nature, it should be potent
- Drug solubility should not be either very high or very low.

Example: Glipizide, Albuterol, Pseudoephedrine, Diltiazem, Verapamil etc.,

Osmotic Agents:

- **Inorganic acid water-soluble salts:**
 - Magnesium chloride or sulfate; lithium, sodium or potassium hydrogen phosphate; sodium or potassium chloride.
- **Water-soluble organic acid salts:**
 - Sodium and potassium acetate, magnesium succinate, sodium benzoate, sodium citrate, sodium ascorbate
- **Carbohydrates:**
 - Manose, sucrose, maltose, lactose
- **Water-soluble amino acids and organic polymeric Osmogens:**

Polyvinyl pyrrolidone, Polyethylene oxide, Methylcellulose, Hydroxy ethyl methyl cellulose, hydroxy propyl methyl cellulose, Sodium carboxy methyl cellulose.

Hydrophilic and Hydrophobic Polymers:

- **Hydrophilic polymers:**
 - Hydroxyl ethyl cellulose, carboxyl methylcellulose, hydroxyl propyl methylcellulose, high molecular weight poly(vinyl pyrrolidone) ,
- **Hydrophobic polymers:**

Ethyl cellulose and wax materials.

Flux Regulating Agents:

- **Hydrophilic substances:**

Polyethethylene glycols (ranges from 300 to 6000 Da), polyhydric alcohols, polyalkylene glycols,

- **Hydrophobic materials:**

Phthalates substituted with an alkyl or alkoxy (e.g., diethyl phthalate or di methoxy ethyl phthalate).

Wicking Agent:

Colloidal silicon dioxide, kaolin, titanium dioxide, alumina, niacinamide. sodium lauryl sulphate (SLS), poly (vinyl pyrrolidone), m-pyrol, bentonite, magnesium aluminium silicate, polyester and polyethylene.

Semi-Permeable Polymers:

Cellulose acetate, cellulose dilacerate, cellulose triacetate, cellulose propionate, cellulose acetate butyrate, ethyl cellulose and eudragits.

Coating Solvent:

Methylene chloride, acetone, methanol, ethanol, isopropyl alcohol, butyl alcohol, ethyl acetate, cyclohexane, carbon tetrachloride, water.

Plasticizers:

Di alkyl phthalates and other phthalates, tri octyl phosphates and other phosphates, alkyl adipates, tri ethyl citrate and other citrates, glycolates, glycerolates, acetates, propionates, myristates, benzoates, sulphonamides and halogenated phenyls.

Pore Forming Agents:

Alkaline metal salts:

such as sodium chloride, sodium bromide, potassium chloride, potassium sulphate, potassium sulphate, potassium phosphate etc.,

Alkaline earth metals:

such as calcium chloride and calcium nitrate,

Carbohydrates:

such as sucrose, glucose, fructose, mannose, lactose, sorbitol, mannitol and diols Polyols such as poly hydric alcohols and polyvinyl pyrrolidone.

Components used in Formulation of Osmotic Drug Delivery System:

1. Semi-Permeable Membrane:

Since the membrane in osmotic systems is semi-permeable in nature, it is possible to select any polymer that is permeable to water but impermeable to solute.¹² Cellulose acetate is a semi-permeable polymer widely used for osmotic pump preparation. It is available in various grades of

acetyl material. In particular, 32% and 38% acetyl content is commonly used. The content of acetyl is defined by the degree of substitution (DS), which is the average number of hydroxyl groups on the polymer's anhydroglucose unit substituted by the substitute group. Some polymers like cellulose esters such as cellulose acetate cellulose diacetate, cellulose triacetate, cellulose propionate, cellulose acetate butyrate, and cellulose ethers like ethyl cellulose can be used for the above purpose.¹³ Besides derivatives of cellulose, some other polymers such as agar acetate, amylase triacetate, poly(vinyl methyl) ether co-polymers, , beta-glucan acetate poly (orthoesters), polyacetals and selectively permeable poly(glycolic acid), poly (lactic acid) derivatives, and Eudragits can be used as semi-permeable film forming materials.¹⁴ Permeability is the key criteria for selecting semi-permeable polymer.¹⁵

2. Hydrophilics and Hydrophobics Polymers:

These polymers are used to formulate osmotic systems to make drugs that contain the core of the matrix. The extremely water-soluble compounds can be concentrated in hydrophobic matrices, and compounds that are moderately water-soluble can be concentrated in hydrophilic matrices for more controlled release. Mixtures of hydrophilic and hydrophobic polymers were commonly used in the formulation of water-soluble drug osmotic pumps.¹⁶ The selection is dependent on the drug's solubility and the amount and rate of drug to be released from the pump. The polymers are either swellable or non-swellable in nature. In the pumps containing relatively water-soluble drugs, swellable polymers are mostly used. Because of their swelling nature they increase the hydrostatic pressure inside the pump, the non-swellable polymers are used for highly water-soluble drugs.¹⁷ Ionic hydrogels such as sodium carboxy methyl cellulose are usually used due to their osmogenic property. Through integrating these polymers into the formulations, more precise controlled release of drugs can be achieved. For this reason it is possible to use hydrophilic polymers such as hydroxy ethyl cellulose, carboxy methyl cellulose, hydroxy propyl methyl cellulose, high molecular weight poly (vinyl pyrrolidone) and hydrophobic polymers such as ethyl cellulose and wax materials.¹⁸

3. Wicking Agents:

A wicking agent is described as a material capable of drawing water into a distribution device's porous network. The wicking agents are those agents that assist with the incoming aqueous fluid to improve the drug's contact surface area. Using the wicking agent helps improve the drug output released from the drug's orifice. A wicking agent has a swellable or non-swellable character.¹⁹ They are distinguished by being able to withstand water physisorption. Physisorption is a type of absorption where the solvent molecules may bind loosely to the wicking agent's surfaces through

Vander Waals interactions between the wicking agent's surface and the adsorbed molecule. The wicking agent's role is to carry water to surfaces inside the tablet's core, thus creating channels or an increased surface area network.²⁰ Sources are silicon dioxide colloidal, PVP and lauryl sulfate sodium.

4. Solubilizing Agent:

Highly water-soluble drugs would demonstrate a high release rate of zero order for the osmotic drug delivery system. Most drugs with low intrinsic solubility in water are therefore poor candidates for osmotic delivery. However, the solubility of drugs can be modulated in the core. Adding solubilizing agents to the core tablet dramatically increases the solubility of the drug.²¹ Classification of Non-swellable solubilizing agents: (i) agents that inhibit drug crystal formation or otherwise act by drug complexation (e.g., PVP, poly(ethylene glycol) (PEG 8000) and β -cyclodextrin), (ii) a high-HLB micellar surfactant, particularly nonionic surfactants (e.g., 20, 60-80 polyoxyethylene or surface-containing polyethylene). Combinations between complexing agents such as polyvinyl pyrrolidone (PVP) and poly(ethylene glycol) and anionic surfactants such as SLS are usually preferred.

5. Osmogens:²²

Osmogens are an essential component of the formulations of osmotic. When the biological fluid gain access through the semi permeable membrane into the osmotic system, osmogens are dissolved in the biological fluid, which causes osmotic pressure buildup inside the pump and forces medicinal products outside the pump through the delivery orifice. These include inorganic salts and carbohydrates. Osmogens are commonly used to achieve maximum osmotic pressure within the device. Eg: - Sodium chloride and potassium chloride.

6. Surfactants.²³

The addition of surfactants to the wall-forming material is particularly useful. They produce an integral composite that can be used to make the device's wall operational. The surfactants act by regulating the surface energy of materials to improve their mixture into the composite during the drug release period and maintain their integrity in the use environment. Typical surfactants such as polyoxyethylene glyceryl ricinoleate, polyoxyethylene castor oil containing ethylene oxide, glyceryl laurates, and glycerol (sorbitone oleate, stearate, or laurate) are included in the formulation.

7. Coating Solvents:²³

Solvents suitable for producing a polymeric solution used to make the osmotic wall involve neutral inorganic and organic solvents that do not damage the core and other materials. Methylene

chloride, acetone, methanol, ethanol, isopropyl alcohol, butyl alcohol, ethyl acetate, cyclohexane, tetrachloride of oil, and water are common solvents. Solvent mixtures such as acetone-methanol (80:20), acetone-ethanol (80:20), acetone-water (90:10), methylene chloride-methanol (79:21) and methylene chloride-methanol water (75:22:3) may be used.

8. Plasticizers.

To modify the physical properties and improve film-forming characteristics of polymers, plasticizers or low molecular weight diluents are added in pharmaceutical coatings. Plasticizers can significantly change the visco-elastic behavior of polymers.²⁴ Plasticizers can turn a hard and brittle polymer into a softer, more flexible material and possibly make it more mechanical stress-resistant.⁹ Plasticizers reduce the temperature of the wall's second order-phase transition or the wall's elastic modules and also increase the coating solvent's workability, flexibility and permeability. In general, 100 parts of costing products are integrated from 0.001 to 50 parts of a plasticizer or a combination of plasticizers. PEG-600, PEG-200, triacetine (TA), ethylene glycol diacetate, triethyl phosphate, dibutyl sebacate, ethylene glycol monoacetate, and diethyl tartrate used in semipermeable membrane formulation as plasticizer.^{25,26}

9. Pore-Forming Agents.

These agents are particularly used in pumps designed for poorly water-soluble drugs and osmotic pumps for in the development of controlled porosity or multiparticulate.²⁷ These pore-forming agents cause microporous membrane formation. The microporous wall may be formed in situ by the leaching of a pore-former during system operation. By fact, the pore-formers can be either inorganic or organic, solid or liquid. For example, alkaline metal salts such as sodium chloride, sodium bromide, potassium chloride, potassium sulphate, potassium phosphate, and so on, alkaline earth metals such as calcium chloride and calcium nitrate, carbohydrates such as , fructose, manose, lactose, sorbitol and mannitol, sucrose, glucose and diols and polyols such as polyhydrates, polyethylene glycols, and polyvinyl pyrrolids Also used to create pore in the membrane are Triethyl citrate (TEC) and triacetine (TA). The permeability of the membrane to the drug is also improved by the addition of HPMC or saccharose.^{28,29}

Types of Osmotically Controlled Drug Delivery Systems:³⁰

1. Single chamber osmotic system:

Elementary osmotic pump

2. Multi chambered osmotic pumps:

2.1 Push-pull osmotic pumps

Sandwiched osmotic pump

Osmotic pump with non expanding second chamber

3. Specific types:

- Controlled-porosity osmotic pumps
- Monolithic osmotic pumps tablet
- Colon targeted Oral Osmotic System (Oros CT)
- Osmotically Brusting Osmotic Pump
- Asymmetrical Membrane Osmotic Tablet
- Liquid Oral Osmotic System
- Effervescent Osmotic pump Tablet
- Multiparticulate Delayed-Release System (osmotic pellet)
- Self Emulsified Osmotic Tablet
- Telescopic capsule for Delayed-Release

1. Single Chamber Osmotic System:

Elementary Osmotic Pump:

They was invented the first osmotic pump in 1974. The elementary osmotic pump is a new drug delivery system that delivers the drug at a controlled rate through an osmotic cycle. Control is based on: a) the water permeation characteristics of a semi-permeable membrane surrounding the formulating agent b) the formulation's osmotic properties. This system includes osmotic active agent surrounded by semi-permeable membrane controlling the release rate of the drug. The system is created by using a tableting machine to compress a medication with a sufficient osmotic pressure into a tablet. The tablet is then coated with a semi-permeable membrane, normally cellulose acetate, and a small hole is drilled through the membrane coating (the size ranges from 0.5 to 1.5 mm). the drilling may be done by Mechanical drilling, laser drilling (CO₂ laser beam with a wavelength of 10.6 μ).³¹ When the dosage form is exposed to the aqueous atmosphere, the core absorbs water osmotically at a controlled rate, which is determined by the osmotic pressure of the core and the water permeability of semi-permeable membrane. The volume of saturated drug solution delivered is equal to the volume of solvent uptake. The rate of the system's solvent distribution is constant as long as the excess solid is present inside the device but the rate decreases parabolistically to zero order once the concentration falls below saturation, which is dispensed at a regulated rate from the membrane's delivery orifice. While 60-80% of the drug is released from the Elementary Osmotic Pump Devices (EOP) at a constant rate, a lag time of 30-60 minutes is observed in most cases as the device hydrates until zero order output from the system begins. Such devices are ideal for providing medicines with reasonable water solubility.³²

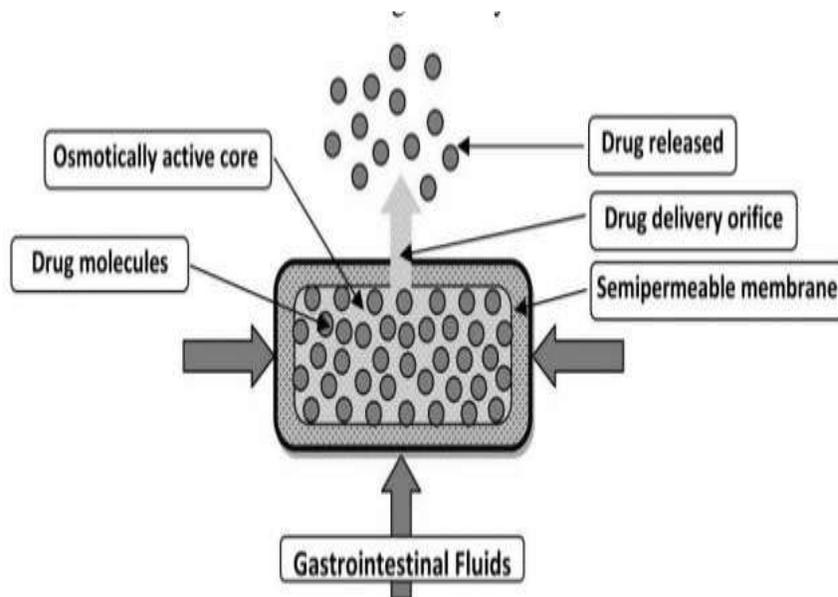


Figure 01: Elementary osmotic pump³³

2. Multi Chambered Osmotic Pumps:

Push Pull Osmotic Pump (PPOP):

The PPOP developed by Alza Corporation consists of two separate compartments (optional) separated by an elastic diaphragm. The upper compartment contains the drug and is connected via a small orifice to the outside environment. There is a polymeric osmotic agent in the lower compartment and there is no orifice for delivery. The drug layer accounts for 60–80% of the tablet weight and 20–40% of the osmotic polymer layer. When the dosage comes into contact with the water, water is absorbed by both the drug layer and the polymer layer. Since the lower compartment has no orifice, it extends and moves the diaphragm into the upper chamber, pushing the drug through the delivery orifice.³⁴ At the same time, the osmotic agent in the non-drug layer draws water into that compartment, causing it to expand volumetrically, and the expansion of the non-drug layer forces the drug suspension out of the delivery orifice.³⁰ The most widely used polymer in the push layer is carbopol (around 20-40 percent wt of the tablet). This device also has a localized release drawback and higher costs.

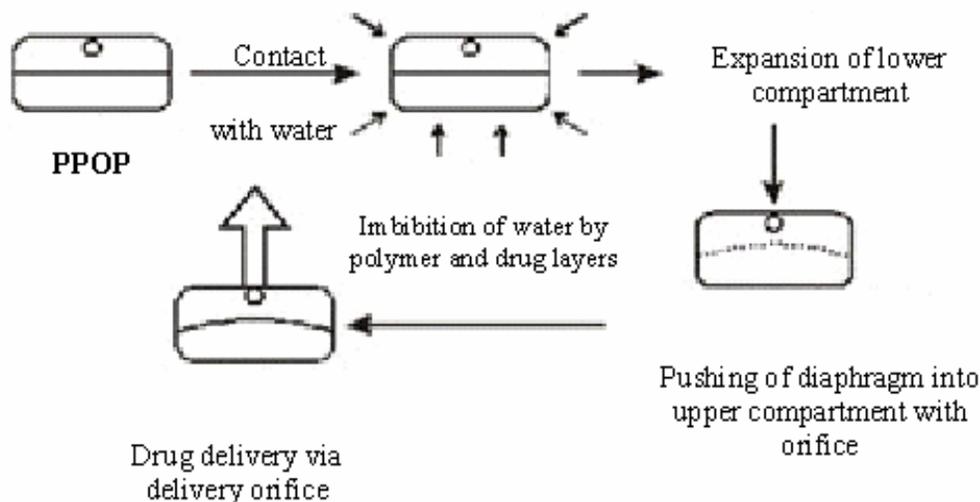


Figure 2: Push pull osmotic pump³⁵

Sandwiched Osmotic Tablets (SOTS):

This consists of a sandwiched polymer push layer between two drug layers and two delivery orifices. The middle push layer containing the swelling agent and the drug is released from the two orifices located on opposite sides of the tablet when inserted in the aqueous environment and therefore SOTS may be ideal for drugs that are likely to cause local inflammation of the gastric mucosa.³⁶

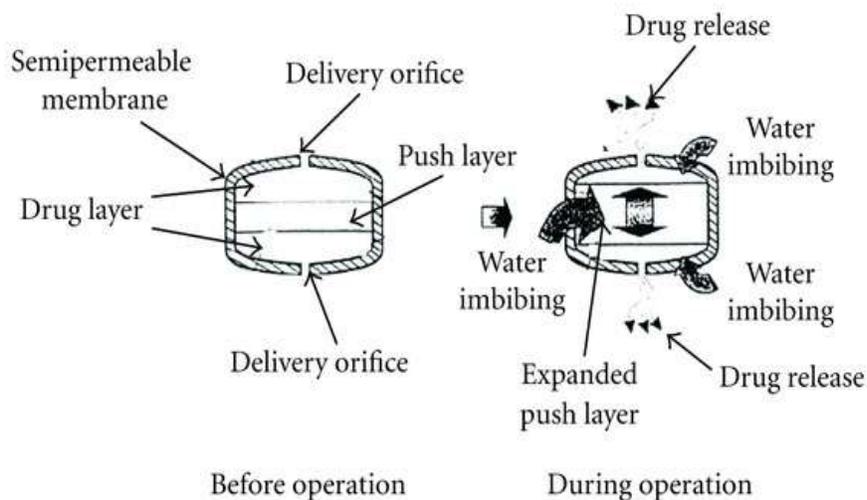


Figure 03: Sandwiched osmotic tablets³⁷

Osmotic Pump with Non Expanding Second Chamber:

The second category of multi-chamber systems involves a machine that incorporates a second chamber that is not expanding. Based on the role of second chamber, this group can be divided into two subgroups. The second chamber is used in one category of these devices to dilute the drug

solution that leaves the devices. This is useful because in some situations, if the drug leaves a saturated solution of the oral osmotic systems, inflammation of the GI tract is a possibility. This type of device consists of two rigid chambers, the first chamber contains an osmotic agent that is biologically inert, such as sugar or a simple salt like sodium chloride, the second chamber contains the drug. In use, water is drawn through the semi-permeable membrane in both chambers. The osmotic agent solution produced in the first chamber then passes through the connecting hole to the drug chamber where it combines with the drug solution before exit through the micro porous membrane forming part of the chamber wall. The device could be used to deliver relatively insoluble drugs.³⁸

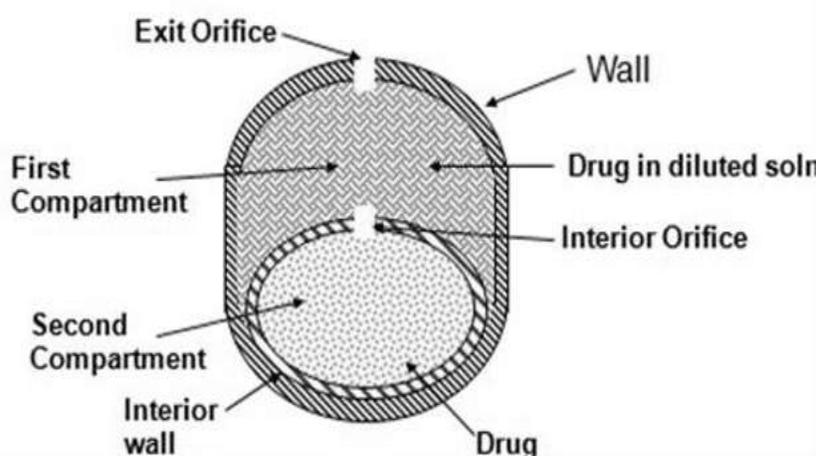


Figure 04: Osmotic pump with non expanding second chamber¹¹

3. Specific Types.

Controlled Porosity Osmotic Pump:

The pump can be made in single or multi-purpose dosage form, in either form, the delivery system consists of a core of the drug surrounded by a membrane with an asymmetric structure. The membrane consists of a phase inversion process controlled by a mixed solvent system evaporation. Membrane is water-permeable, but it is impermeable to solutions and insensitive pore shaping additives that are spread across the surface. Low water-soluble additive amounts are leached from polymer products that were water-permeable but remained insoluble when exposed to water. Then the resulting sponge-like structure formed of interest the controlled porosity walls and was substantially permeable to both water and drug agents dissolved. The release rate of these types of systems depends on the factors such as water permeability of the semi-permeable membrane, the thickness of the coating, the amount of soluble components in the coating, the solubility of the drug in the tablet core and the difference in osmotic pressure across the surface, but is independent

of the pH and agitation of the release medium, the rate of release of drugs and the osmotic pressure. All these variable are under the designer's influence and do not differ under physiological condition, resulting in the above-mentioned robust results.

The rate of flow of water into the device can be given as;³⁹

$$dv/ dt = Ak / h (Dp-DR)$$

Where k = Membrane permeability, A = Area of the membrane, Dp = Osmotic pressure difference,

DR = Hydrostatic pressure difference.

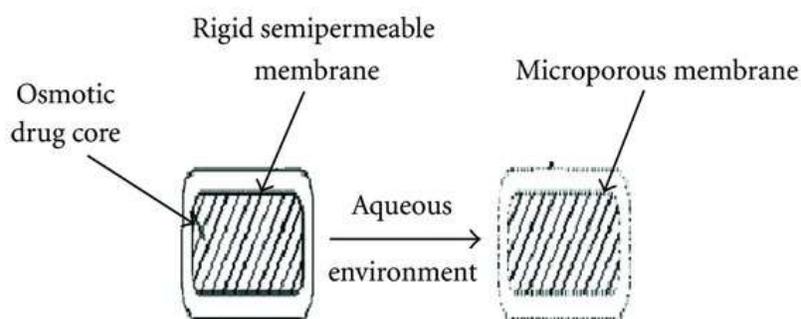


Figure 05: Controlled porosity osmotic pump⁴⁰

3.2 Monolithic Osmotic System:

The monolithic osmotic method is a basic dispersion in polymer matrix of water-soluble agent. Polymers encapsulate the particles of the drug. When the system comes into contact with the aqueous environment, the active agents ' water imbibitions rupture the polymer matrix capsule that surrounds the drug and thus release it into the external Environment. Initially this process takes place in the outer environment of the polymer matrix, but gradually progresses in a sequential fashion into the inside of the matrix. Such structures control the kinetics of drug delivery in zero order. The osmotic pressure is the main principle.³⁹

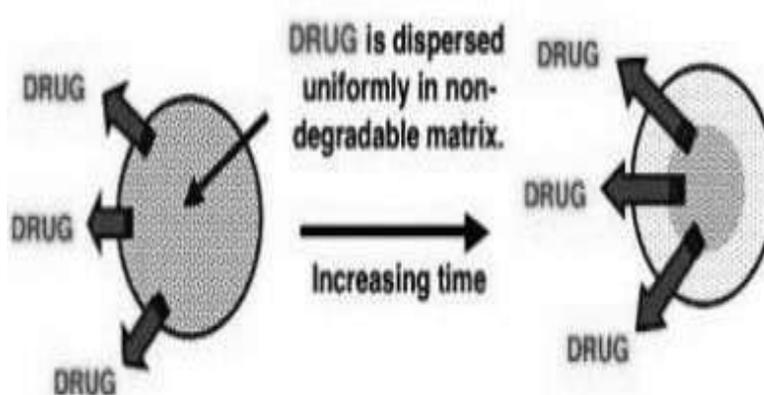


Figure 06: Monolithic osmotic system⁹

Colon Targeted Oral Osmotic System (OROS-Ct):

The system can be used once or twice a day to administer medications to the colon in a controlled manner. The device is fitted with 5-6 enteric coating and osmotic push-pull units loaded with hard gelatin capsule for controlled delivery of colonic drugs.⁴¹ When gelatin capsule shell dissolves upon contact with GI fluids, the outer shell of the product prevents the entry of fluid from the stomach and dissolves after it reaches the intestine. The water imbibes to the core and the swelling of push compartment takes place. At the same time, the flowable gel is formed that is forced out at a predetermined rate via the delivery orifice.⁴²

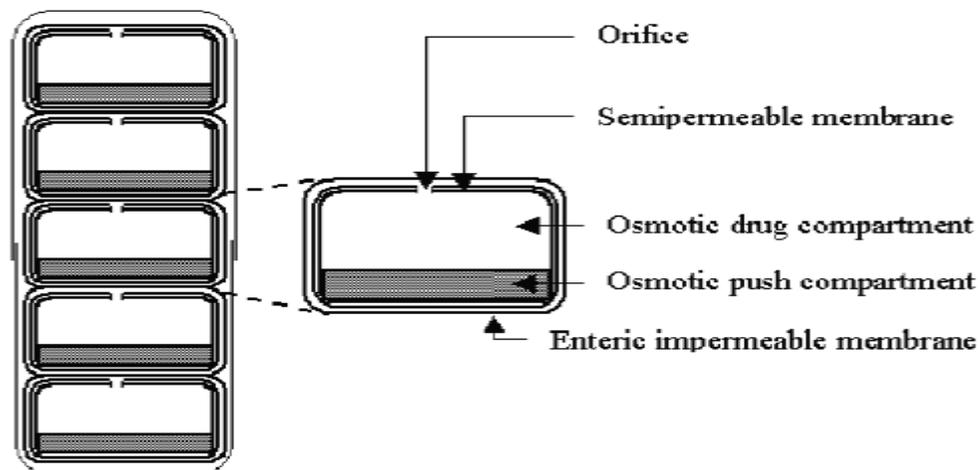


Figure 07: Colon targeted oral osmotic system⁴³

Osmotically Bursting Osmotic Pump:

Baker developed a controlled-release delivery system using an osmotic bursting mechanism. The delivery orifice is absent in this system and the orifice scale is small than the standard osmotic system (EOP). When placed in a watery environment, water is absorbed and hydraulic pressure is built up inside until the wall breaks and the contents are released into the environment. The drug release can be controlled by the thickness as well as the area of the semi-permeable membrane. This method is useful in providing pulsed release.⁴⁴

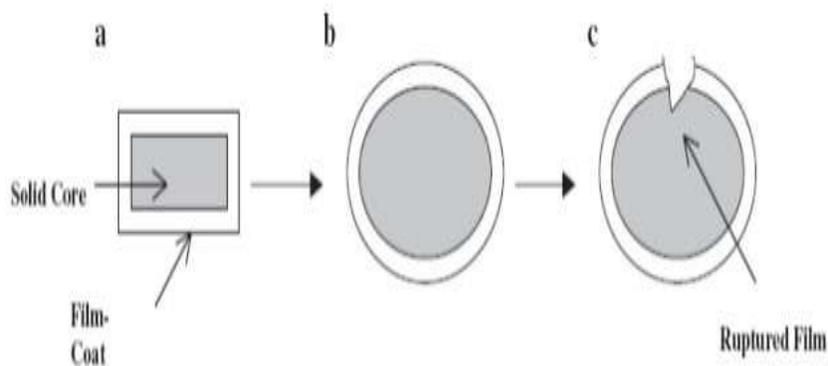
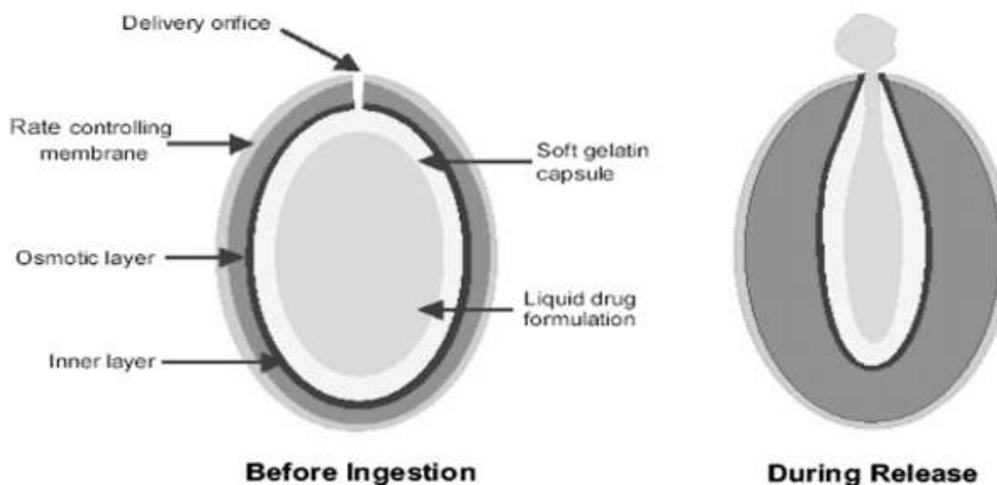


Figure 08: Osmotically brusting osmotic pump³³**3.5 Asymmetrical Membrane Osmotic Tablet:**

Asymmetric membrane capsules consists of a product that comprises a center surrounded by a membrane that has an asymmetric structure, i.e. it has a relatively thin, dense region protected by a thicker, porous area. Unlike a conventional gelatin capsule, the capsule wall is made of a water-insoluble polymer such as cellulose acetate; the asymmetric membrane capsule does not dissolve instantly but provides a sustained release of the active ingredient in the capsule.⁴⁵

3.6 Liquid Oral Osmotic System:

Liquid OROS is designed to supply medications as liquid formulations, combining the advantages of extended release with high bioavailability. Such devices are ideal for the controlled delivery of formulations of liquid drugs including lipophilic self-emulsifying formulations (SEF). These are of three types:-LOROS hard cap, LOROS soft cap, Delayed liquid bolus delivery system A liquid drug layer, an osmotic engine or push layer and a semi-permeable membrane coating are included in each of these devices. When the system gets in contact with the aqueous environment, water gain access through the membrane and causes the stimulation of the osmotic layer The expansion of the osmotic layer results in the creation of hydrostatic pressure within the device, forcing the liquid solution from the delivery orifice to be delivered.⁴⁶ Alza has developed liquid delivery osmotic systems. It technology enables insoluble drugs to be administered in aqueous fluids and is recorded to improve drug permeability.⁴⁷

**Figure 09: Liquid oral osmotic system**⁴⁸**3.7 Effervescent Osmotic Tablet (EOT):**

In this system, the carbon dioxide is formed by effervescent compounds in a dosage form that reacts with acid in the outer environment. This gas expands and dispenses the precipitate drug and

prevents orifice blockage. This system can precipitate at the gastric pH and block the delivery orifice for poorly soluble drug at low pH. In this method, sodium bicarbonate is normally used.⁴⁹

3.8 Multiparticulate Delayed-Release System:

Pellets containing a pure drug with or without an osmotic agent are coated with a semi-permeable membrane such as cellulose acetate in this system. Water penetrates into the core when this device comes into contact with the aqueous atmosphere and forms a saturated solution of soluble materials. The gradient of osmotic pressure causes a water flow, leading to rapid membrane expansion and pores formation. The release of osmotic ingredients and the drug through these pores tends to follow zero-order kinetics.⁵⁰

3.9 Self Emulsified Osmotic Tablet:

Self-emulsifying agents were added to the tablet-core composition in the case of slightly soluble or practically insoluble drugs. There are approximately 40 percent of drugs available that are poorly soluble in water. Self-emulsifying system improves drug bioavailability, controlled release rate, and by self-emulsifying agent makes plasma concentrations more stable. This emulsifies drugs that are hydrophobic. For this purpose, typical surfactants such as polyoxyethylene castor oil containing ethylene oxide polyoxyethylene glyceryl recinoleate, glyceryl laureates, glycerol (sorbiton oleate, stearate or laurate), etc.⁵¹

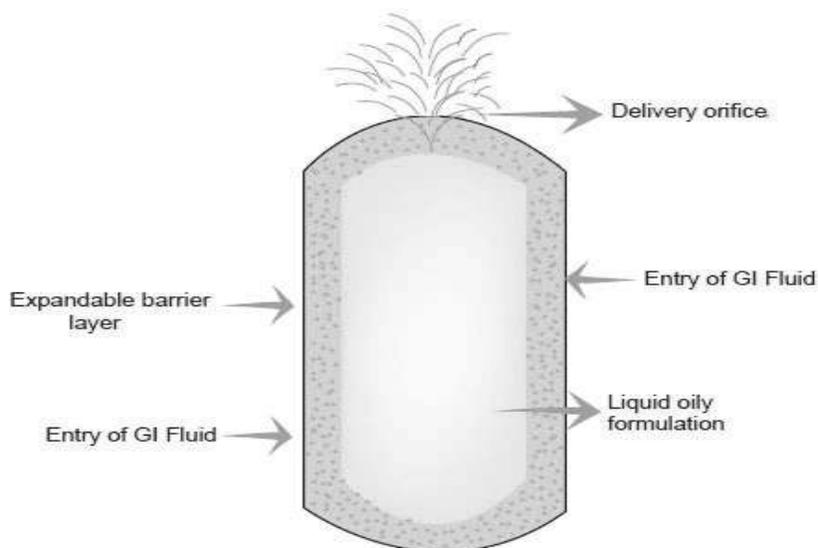


Figure 10: Self emulsified osmotic tablet⁵²

3.10 Telescopic Capsule for Delayed Release:

This device consists of two chambers, the first containing the drug and an escape port, the second containing an osmotic engine, a wax-like layer separating the two parts. To assemble the delivery device, by manual or automated filling process, the desired active agent is positioned in one of the

pieces. The bilayer tablet with the osmotic engine is placed in the capsule's completed cap section with the convex osmotic layer pointing to the cap's closed end and the barrier pointing to the cap's closed end and the cap's exposed barrier layer. The filled vessel's open end is fitted within the open end of the cap, and the two pieces are compressed together until the cap, osmotic bilayer tablet and vessel fit together tightly.³⁰ When fluid is immersed in the dispensing device's casing, the osmotic engine expands and exerts pressure on the first and second wall parts connected to the slidable. The volume of the reservoir containing the active agent is kept constant during the delay time, due to which there is a marginal pressure differential between the reservoir's usage environment and interior. Consequently, the net flow of the environmental fluid driven by pressure enters the reservoir is minimal.⁵³

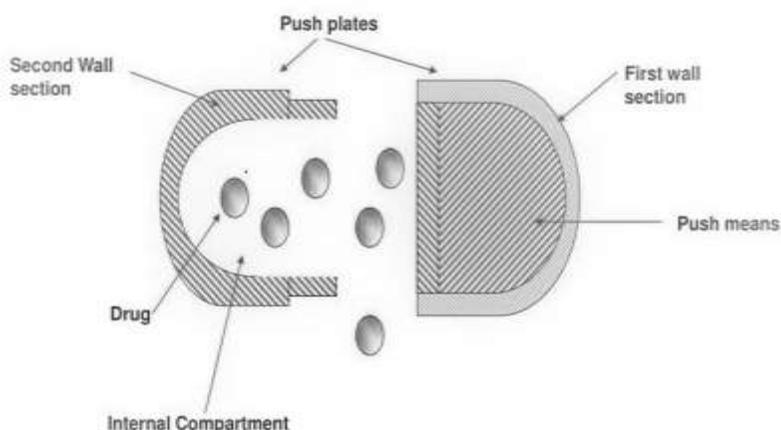


Figure 11: Telescopic capsule for delayed release⁹

Table 1: Examples of some marketed brand of Osmotic drug delivery system²³

Product name	Chemical name	Type of delivery	Developer/marketer
Acutrim	Phenylpropanolamine	Elementary pump	Alza/heritage
Alpress LP	Prazosin	Push-pull	Alza/Pfizer
Cardura xl	Doxazosin	Push-pull	Alza/Pfizer
Covera hs	Verapamil	Push-pull	Alza/gd Searle
Ditropan xl	Oxybutinin chloride	Push-pull	Alza/UCB pharma
Efidac 24	Pseudoephedrine	Elementary pump	Alza/Novartis
Glucotrol xl	Glipizide	Push-pull	Alza/Pfizer
Minipressxl	Prazosine	Push-pull	Alza/Pfizer
Procardiaxl	Nifedipine	Push-pull	Alza/Pfizer
Teczam	Enapril and diltiazem	Elementary pump	Merck/Aventis

CONCLUSION:

Osmotic drug delivery system in the delivery of oral drugs can be a promising tool. In osmotic delivery systems, osmotic pressure provides the driving force for the release of drugs. Increasing

pressure from water imbibition inside the device causes the drug to be released from the system. Optimization of these parameters can control the release of drug as per the time period require. By using this technique, the release may be pulsed for the specific time in chronotherapy. The major advantages include accurate control over zero-order or other patterned release over an extended period of time. consistent release rates can be achieved regardless of the delivery site's environmental factors. Controlled delivery via osmotic systems also reduces the side-effect profile by moderating the typical blood plasma peaks of conventional dosage forms.

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REFERENCE:

1. Ratnaparkhi, M. P. & Gupta, J. P. Sustained Release Oral Drug Delivery System - An Overview. *Int. J Pharm Res Rev.* 2013; 2(3): 11-21.
2. Khavarel NB, Dasankoppa F.S, Najundaswamy NG, A Review on Key Parameters and Components in Designing of Osmotic Controlled Oral Drug Delivery Systems. *Ind J Novel Drug Del., India.* 2010; 2(4): 122-126.
3. Gupta P.B, Thakur N, Jain N.P, Osmotically Controlled Drug Delivery System with Associated Drugs. *J Pharm Pharm Sci, India.* 2010; 13(3): 571-580.
4. Verma R.K, Krishna D.M, Garg S. "Formulation aspects in the development of osmotically controlled oral drug delivery systems," *J Control Release*, vol. 79, no. 1-3, pp. 7-27, 2002.
5. Kaushal A.M, Garg G. *Pharm. Tech.*,2003, 27, 38-44 [94].
6. Santus G, Baker RW. *J Control Release*,1995, 35(1),1-21.
7. Aulton's Pharm; The Design and Manufacture of Medicines,3rd ed. Philadelphia, USA: Churchill Livingstone Elsevier. pp: 99-102.
8. Cortese R, Theeuwes F. Osmotic device with hydro gel driving member, US Patent No. 4,327,725 (1982).
9. Neetu Khatri, Sarika Nikam, Ajay Bilandi. Oral Drug Delivery System: A Review *IJPSR.* 2016; 7(6); 2302-2312
10. Sharma S, Singh SP, Bhardwaj S, Gaurave K,Gupta GD. Latest Reviews [Internet]. 2008; 6.
11. Sowjanya M, Venkata Prasada Rao CH, Srinivasa Babu, Pallavi k. Osmotic Drug Delivery system; A Review *Inventi Rapid.* 2017 (3) : 1-9.

12. Lindstedt B, Ragnarsson G, Hjartstam J. "Osmotic pumping as a release mechanism for membrane-coated drug formulations." *Int. J Pharm*, vol. 56, no. 3, pp. 261–268, 1989.
13. Seminoff L.A, Zentner G.M. "Cellulosic coating," US patent 5,126,146, 1992.
14. Jensen J.L, Appel L.E, Clair J.H, Zentner G.M. "Variables that affect the mechanism of drug release from osmotic pumps coated with acrylate/methacrylate copolymer latexes." *J Pharm Sci*. 1995; 84(5): 530-533.
15. Theeuwes F. "Elementary osmotic pump." *J Pharm Sci*. 1975; 64(12): 1987-1991.
16. Zentner G.M, Rork G.S, Himmelstein K.G. "The controlled porosity osmotic pump," *J Control Release*. 1985; 1(4): 269-282.
17. Dong L, Shafi K, Wan J, Wong P.A. "novel osmotic delivery system: L-OROS Soft cap," in *Proceedings of the International Symposium on controlled Release of Bioactive Materials*, Paris, France, 2000.
18. Parmar N.S, Vyas S.K. *Adv Control Novel Drug Del*, CBS. 2008.
19. Ghosh T, Ghosh A, "Drug delivery through osmotic systems—an overview," *J Appl Pharm Sci*. 2011; 2: 38-49
20. Rudnic E.M, Burnside B.A, Flanner H.H, et al., Patent 6,110,498, 2000.
21. McClelland G.A, Sutton S.C, Engle K, Zentner G.M. "The solubility-modulated osmotic pump: in vitro/in vivo release of diltiazem hydrochloride," *Pharm Res*. 1991; 8(1): 88-92.
22. Jerzewski R.J, Chien Y.W, "Osmotic drug delivery," in *Treatise Control Drug Del: Fundamentals, Optimization, Application*, A. Kydonieus, Ed., pp. 225–253, Marcel Dekker, New York, NY, USA, 1992.
23. Rajesh Keraliya A, Chirag Patel, Pranar Patel, Vipul Keraliya, Tejal Soni G, Rajnikant Patel C, et al. *Osmotic Drug Delivery System as a part of Modified Release Dosage Form*. ISRN Pharmaceutics. 2012.
24. Guo J.H, "Effects of plasticizers on water permeation and mechanical properties of cellulose acetate : antiplasticization in slightly plasticized polymer," *Drug Dev Ind Pharm*. 1993; 19(13): 1541–1555.
25. Bindschaedler C, Gurny R, Doelker E, "Mechanically strong films produced from cellulose acetate latexes," *J Pharm Pharmacol*. 1987; 39(5): 335–338.
26. Guo J.H, "An investigation into the formation of plasticizer channels in plasticized polymer films," *Drug Dev Ind Pharm*. 1994; 20(11): 1883-1893.

27. Zentner G.M, Rork G.S, Himmelstein K.J. "Osmotic flow through controlled porosity films: an approach to delivery of water soluble compounds," J Control Release. 1985; 2:217–229.
28. Zentner G.M, Rork G.S, Himmelstein K.J. "Controlled porosity osmotic pump," US patent 4,968,507, 1990.
29. Kelbert M, Bechard S.R. "Evaluation of a cellulose acetate (CA) latex as coating material for controlled release products," Drug Dev Ind Pharm. 1992; 18(5): 519–538.
30. Sharma S. 2008. Osmotic Drug Delivery System. Pharmainfo.net. 6(3).
31. Lu Xu, Sanming L, Hisakazu S. Preparation and evaluation in vitro and in vivo of captoprilmn elementary osmotic pump tablets. Asian J Pharm Sci. 2006; 1 (34): 236-245.
32. Gadwal P, Rudrawal P, Ahamad D, Ahmed A. A review on osmotically regulated devices. Int J Pharm Life Sci. 2010; 1(6): 302-312.
33. Bhagat Babasaheb, Hapse Sandip, Darkunde Sachin. Osmotic Drug Delivery System. An overview. IJPPR 2014 ; 2(1) : 29-44.
34. Vincent M, Joerg O, Nicoletta L, Robert G. Oral osmotically driven systems: 30 years of development and clinical use. Eur J Pharm Biopharm. 2009; 73: 311-323.
35. Osmotically Controlled Oral Drug Delivery Systems: A Review - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Mechanism-of-Drug-Delivery-from-a-Push-Pull-Osmotic-Pump-PPOP_fig3_200923983 [accessed 16 Jan, 2020]
36. Liu L, Khang, G, Rhee J.M, Lee, H.B. Monolithic osmotic tablet system for nifedipine delivery. J Controrl Release. 2000; 67: 309-322.
37. Tanmoy Ghosh, Amitava Ghosh. Drug Delivery Through Osmotic Systems – An overview. J Appl Pharm Sci. 2011; 1(02) : 38-49.
38. Herbig S.M, Cardinal J.R, Korsmeyer R, WandSmith K.L. Assymetric-membrane tablet coatings for osmotic drug delivery. J Controrl Release. 1995; 35: 127-136.
39. Zentner G.M, Rork G.S, Himmelstein K.J. Osmotic Flow Through Controlled Poroslty Films, An Approach To Delivery Of Water Soluble Compounds. J Control Release. 1985;1: 269–282.
40. Chinmaya Keshari Sahoo, Surepalli Ram Mohan Rao, MuvvalaSudhakar, Nalini Kanta Sahoo. J Chem Pharm Res. 2015; 7(7): 252-273.
41. Gupta R.N, Gupta R, Basniwal P.K, Rathore G.S. Osmotically Controlled Oral Drug Delivery Systems: A Review. Int J Pharm Sci. 2009; 1(2): 269275.

42. Theuwes F, Wong P.S, Burkoth T.L, Fox D.A, Bicek P.R. “In: colonic drug absorption and metabolism”, Marcel Decker, New York, 1993; 137-158.
43. Primary and novel approaches for colon targeted drug delivery: A review - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Cross-section-of-the-OROS-CT-colon-targeted-drug-delivery-system_fig3_220043126 [accessed 14 Jan, 2020]
44. Amir M, Joseph B. Release of Cyclobenzaprine Hydrochloride from Osmotically Rupturable Tablets. *Drug Dev Ind Pharm.* 2002; 28: 695– 701.
45. Bhanushali R, Rajeshri W, Amrita B. Monolithic Osmotic Tablets for Controlled Delivery of Antihypertensive Drug. *J Pharm Innov.* 2009; 4:63–70.
46. Verma R.K, Divi M.K, Garg S. Formulation aspects in the development of osmotically controlled oral drug delivery systems. *J Control Release.* 2002; 79: 7– 27.
47. Kaushal A.M, Garg S. An Update on Osmotic Drug Delivery Patents. *Pharm Tech .* 2003; 13(1):8-97.
48. Javad Shokri, Parinaz Ahmadi, Parisa Rashidi, Mahbobeh Shahsavari, Ali Rajabi-Siahboomi, Ali Nokhodchi. *Eur J Pharm Biopharm.* 2008; 68: 289-297.
49. Xio-dong Lee, Wei-san Pan, Shoe-fan Lee, Li-ju Wu, 2004. Studies on controlled release effervescent osmotic pump tablet from traditional Chinese medicine compound recip, *J control release*, 96: 359-367.
50. Schultz P, Kleinebudde P. A new multiparticulate delayed release system. Part I: Dissolution properties and release mechanism. *J Control Release.* 1997; 47:181-189.
51. Khavare N.B, Fatima S. D, Najundaswamy N.G. A Review on Key Parameters and Components in Designing of Osmotic Controlled Oral Drug Delivery Systems. *Ind J Novel Drug del.* 2010; 2(4): 122-131.
52. Recent Advancements in Self-emulsifying Drug Delivery Systems (SEDDS) - Scientific Figure on Research Gate. Available from: https://www.researchgate.net/figure/A-typical-depiction-of-an-oral-osmotic-self-emulsifying-system_fig6_259737313 [accessed 16 Jan, 2020]
53. Gohel M. Parikh R.K, Shah N.Y. Osmotic Drug Delivery: An Update. *Pharmainfo.net.* 2009; 7(2):47-50.

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