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OSMOTIC DRUG DELIVERY SYSTEM: AN OVERVIEW

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ABSTRACT

Conventional drug delivery systems have little control over drug release and almost no control over the effective concentration at the target site. The major problem associated with conventional drug delivery system is unpredictable plasma drug concentrations. In recent years, considerable attention has been focused on the development of novel drug delivery systems (NDDS). Osmotically controlled drug delivery systems (ODDS) are a type of NDDS which based on osmotic pressure for controlled delivery of active agent. These systems are used for both oral administration and implantation. These systems utilize osmosis as the major driving force for drug release. Adequate water solubility of the drug is essential for osmotic drug delivery system. Osmotic drug delivery devices are composed of an osmotically active drug core, which is surrounded by a rate controlling membrane. The release of drug(s) from osmotic systems is affected by various formulation factors such as osmotic pressure of the core component(s), solubility and size of the delivery orifice, and nature of semi permeable membrane. Different types of osmotic systems have been developed implantable and oral. This review focuses on types of ODDS and various formulation aspects from the systems and concerned with the study of drug release systems.

INTRODUCTION: [1, 2, 3]

Osmotic drug delivery has come a long way since Australian physiologists Rose and Nelson developed an implantable pump in 1955. Osmotic drug delivery uses the osmotic pressure for controlled delivery of drugs by using osmogens (for up to 10 – 16 hrs). Osmotic systems for controlled drug-delivery applications are well established, both in human pharmaceuticals and in veterinary medicine. Osmotic drug-delivery systems suitable for oral administration typically consist of a compressed tablet core that is coated with a semipermeable membrane coating. This coating has one or more delivery ports through which a solution or suspension of the drug is released over time. The core consists of a drug formulation that contains an osmotic agent and a water swellable polymer. The rate at which the core absorbs water depends on the osmotic pressure generated by the core components and the permeability of the membrane coating. As the core absorbs water, it expands in volume, which pushes the drug solution or suspension out of the tablet through one or more delivery ports.

In the recent years, pharmaceutical research has led to the development of several novel drug delivery systems. The role of drug development is to take a therapeutically effective molecule with sub-optimal physicochemical and/or physiological properties and develop an optimized product that will still be therapeutically effective. The drug release can be modulated by different ways but the most of novel drug delivery systems are prepared using matrix, reservoir or osmotic principle. In matrix systems, the drug is embedded in a polymer matrix and the release takes place by partitioning of drug into the polymer matrix and the surrounding medium. In contrast, reservoir systems have a drug core surrounded by a rate controlling membrane.

The osmotic pressure is proportional to concentration and temperature and the relationship can be described by following equation.

$$\Pi = Ø\ c\ RT$$

Where, Ø = Osmotic pressure,

Π = osmotic coefficient,

c = molar concentration,

R = gas constant,

T = Absolute temperature

DEFINATIONS: [4]

- **Osmolarity** is the number of osmoles per liter of solution.
- **Osmosis** can be defined as the net movement of water across a selectively permeable membrane driven by a difference in osmotic pressure across the membrane. It is driven by a difference in solute concentrations across the membrane that allows passage of water, but ejects most solute molecules or ions. Osmotic pressure is the pressure which, if applied to the more concentrated solution, would prevent transport of water across the semipermeable membrane.
- **Osmolality** is the number of osmoles per Kg of water.
- **Osmotic pressure** can be defined the pressure applied to the higher-concentration side to inhibit solvent flow.

OSMOSIS: [5]

Process of movement of the solvent from the lower concentration of solution to the higher concentration of the solution through the semipermeable membrane. Osmosis is the process that can control the drug delivery system. Osmotic pressure created due to imbibitions of fluid from external environment into the dosage form regulates the delivery of drug from osmotic device. Rate of drug delivery from osmotic pump is directly proportional to the osmotic pressure developed due to imbibitions of fluids by osmogen. Osmotic pressure is a colligative property of a solution in which the magnitude of osmotic pressure of the solution is independent on the number of discrete entities of solute present in the solution. Hence the release rate of drugs from osmotic dispensing devices is dependent on the solubility and molecular weight and activity coefficient of the solute (osmogent).

HISTORY OF OSMOTIC DRUG DELIVERY SYSTEM : [6]

About 75 years after discovery of the osmosis principle, there was clear in the design of drug delivery systems. Rose and Nelson, the Australian scientists, were initiators of osmotic drug delivery. In1955- they developed an implantable pump, which consisted of three chambers: a drug chamber, a salt chamber contains excess solid salt, and a water chamber. In1975- the elementary osmotic pump for oral delivery of drugs was introduced. The pump consists of an

osmotic core containing the drug, surrounded by a semipermeable membrane with a delivery orifice. When this pump is exposed to water, the core imbibes water osmotically at a controlled rate, determined by the membrane permeability to water and by the osmotic pressure of the core formulation. As the membrane is non-expandable, the increase in volume caused by the imbibitions of water leads to the development of hydrostatic pressure inside the tablet. This pressure is relieved by the flow of saturated solution out of the device through the delivery orifice. In1970s- implantable osmotic pumps were a major breakthrough to deliver wide range of drugs and hormones, including peptides at constant and programmed rate.

Advantages of Osmotic Drug Delivery System: [7, 8, 9]

1. Higher release rates are possible from osmotic systems than with conventional diffusion based drug delivery systems
2. The delivery rate of zero-order is achievable with osmotic systems.
3. For oral osmotic systems, drug release is independent of gastric pH and hydrodynamic conditions.
4. The release rate of osmotic systems is highly predictable and can be programmed by modulating the release control parameters.
5. Extended release of a large amount of highly water-soluble drug by utilizing counter polymer in polyethylene oxides
6. A high degree of in vivo- in vitro correlation (IVIVC) is obtained in osmotic systems.

Disadvantages of Osmotic Drug Delivery System: [8, 9]

1. Cannot crush or chew products: Osmotic pump tablet should not be crushed or chewed as it can lead to loss of the ‘slow release’ characteristics as well as toxicity.
2. Release rate: The drug release rate can be altered by food and gastric transit time; as a result differences may arise in the release rate between doses.

LIMITATION: [10]

1. It may cause irritation or ulcer due to release of saturated solution of drug.
2. Special equipment is required for making an orifice in the system.

3. Residence time of the system in the body varies with the gastric motility and food intake.

Basic Components of Osmotic System:

- Drug
- Coating agent
- Wicking agent
- Semipermeable membrane
- Pore forming agent
- Plasticizers
- Osmotic agent

Drug: [11, 12]

Drugs which have short biological half-life (2-6 hrs) and which are used for prolonged treatment are ideal candidate for osmotic systems. Various drug candidates such as Diltiazem hydrochloride, Carbamazepine, Metoprolol, Oxprenolol, Nifedipine, Glipizide, etc. are formulated as osmotic delivery.

Drug having following characteristics are suitable for formulation

1. It should have short half-life.
2. Prolonged release of drug should be desired.
3. It should be potent in nature.
4. Solubility of drug should not be very high or very low.

Coating agent: [13]

Solvents suitable for making polymeric solution that is used for manufacturing the wall of the osmotic device include inert inorganic and organic solvents that do not adversely harm the core, wall and other materials. The typical solvents include methylene chloride, acetone, methanol, ethanol, isopropyl alcohol, butyl alcohol, ethyl acetate, cyclohexane, carbon tetrachloride, water etc. The mixtures of solvents such as acetone-methanol (80:20), acetone-ethanol (80:20), acetone-water (90:10), methylene chloride-methanol (79:21), methylene chloride-methanol-water (75:22:3) etc. can be used.

Wicking agent: [14]

Wicking agent is defined as a material with the ability to draw water into porous network of a delivery device.

- A wicking agent is of either swellable or non-swellable nature.
- They are characterized by having the ability to undergo physiosorption with water.
- Physiosorption is a form of absorption in which the solvent molecules can loosely adhere to surface of the wicking agent via Van der waals interactions between the surface of the wicking agent and the absorbed molecule.
- The function of the wicking agent is to carry water to surfaces inside the core of the tablet there by creating channels or a network of increased surface area.
- Materials, which suitably for act as wicking agents include colloidal silicon dioxide, kaolin, titanium dioxide, alumina, niacinamide, sodium lauryl sulphate (SLS), low in weight poly (vinyl pyrolidone) PVP , m-pyrol, bentonite, magnesium aluminium silicate, polyester and polyethylene. SLS, colloidal silica and PVP are non swellable wicking agents.

Semi permeable membrane: [14]

An important part of the osmotic drug delivery system is the semipermeable membrane housing. Therefore, the polymeric membrane selection is important to the osmotic delivery formulation. The membrane should possess certain characteristics, such as

- Sufficient wet strength and water permeability
- Should be biocompatible.
- Rigid and non-swelling
- Should be sufficient thick to withstand the pressure within the device.

Any polymer that is permeable to water but impermeable to solute can be used as a coating material in osmotic devices. Some of the polymers that can also used.

Pore forming agent: [15]

The pore-forming agents cause the formation of micro porous membrane. The micro porous wall may be formed in situ by a pore-former by its leaching during the operation of the system. The

pore-formers can be inorganic or organic and solid or liquid in nature. For example, alkaline metal salts such as sodium chloride, sodium bromide, potassium chloride, potassium sulphate, potassium phosphate etc., alkaline earth metals such as calcium chloride and calcium nitrate, carbohydrates such as sucrose, glucose, fructose, mannose, lactose, sorbitol, and mannitol and, diols and polyols such as poly hydric alcohols, polyethylene glycols and polyvinyl pyrrolidone can be used as pore forming agents.

Plasticizers: [16]

Different types and amount of plasticizers used in coating membrane also have a significant importance in the formulation of osmotic systems. They can change visco-elastic behaviour of polymers and these changes may affect the permeability of the polymeric films. Some of the plasticizers used are as below:

- Polyethylene glycols
- Ethylene glycol monoacetate
- Diacetate- for low permeability
- Tri ethyl citrate
- Diethyl tartarate or Diacetin- for more permeable films

Osmotic agent: [17, 18]

These are also known as osmogens or osmogents and are used to create osmotic pressure inside the system. When the solubility of drug is low then the drug will show zero order release but at a slow rate. To enhance the release rate osmotic agent is added in the formulation. Osmotic agent creates a very high osmotic pressure gradient inside the system and increases release rate of drug.

Some of the commercially used osmotic agents:

Sodium chloride, Fructose, Sucrose, Potassium chloride, Xylitol, Sorbitol, Citric acid, Dextrose, Manitole and Lactose.

Some Mixture Used As an Osmotic Agent:

- Dextrose +Fructose
- Lactose +Fructose

- Sucrose+ Fructose
- Lactose +Dextrose
- Mannitol +Fructose
- Mannitol +Dextrose
- Dextrose +Sucrose
- Mannitol +Sucrose

CLASSIFICATION OF OSMOTIC DRUG DELIVERY SYSTEM:

1) Single Chamber Osmotic Pumps

   a) Elementary Osmotic Pumps

2) Osmotic Pump with Non-Expanding Second Chamber

3) OROS Push-Stick Technology

4) Osmotic bursting osmotic pump

5) Modified Osmotic Pumps

   a) Controlled porosity osmotic pumps (CPOP)

6) Telescopic capsule for delayed release

7) Sandwiched osmotic tablet (SOTS)

8) Liquid OROS controlled release system (L-OROS)

   a) Liquid OROS Soft cap
   b) Liquid OROS hard cap

9) Multiple Chambers Osmotic Pumps

   a) Push-pull osmotic pump (PPOP)

1) Single Chamber Osmotic Pumps:

a) Elementary Osmotic Pumps [19]

Composition- osmotic core (containing drug with or without an osmagent) coated with a semipermeable membrane (SPM) and a small orifice is created in the membrane.

Mechanism of Action-Imbibes water through the SPM because of the osmotic pressure gradient and forms a saturated solution inside the device. This increases the hydrostatic pressure inside the tablet and forces the saturated drug solution through the orifice present in the membrane.

Advantage -Suitable for delivery of drugs having moderate water solubility

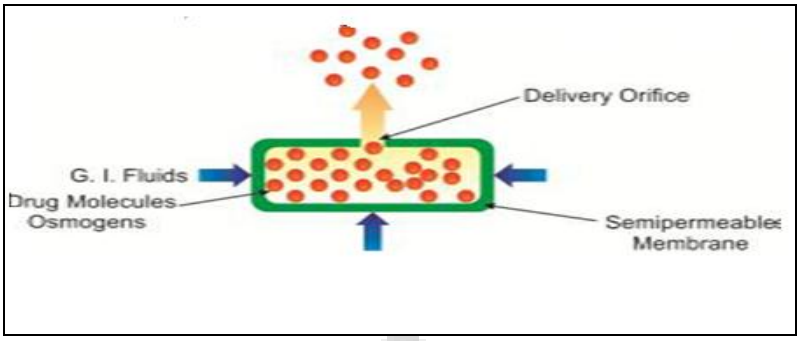

Fig.1- Elementary Osmotic Pumps

2) Osmotic Pump with Non-Expanding Second Chamber: [20]

Composition-Multi-chamber devices comprise of systems containing a non-expanding second chamber.

Mechanism of Action- Purpose of second chamber is either dilution of drug solution leaving the device (particularly useful in handling drugs with high incidence of GI irritation) or simultaneous delivery of two drugs

Advantages- Relatively insoluble drugs can also be delivered.

3) OROS Push-Stick Technology: [21]

Composition-It consists of a bilayer capsule shaped tablet.

Mechanism of Action- When the dosage form comes in contact with the aqueous environment, both compartments imbibe water simultaneously. Because the lower compartment is devoid of any orifice, it expands and pushes the diaphragm into the upper drug chamber, thereby delivering the drug via the delivery orifice.

Advantages- Deliver both highly water-soluble (oxybutynin hydrochloride) and practically water-insoluble (nifedipine, glipizide) drugs.

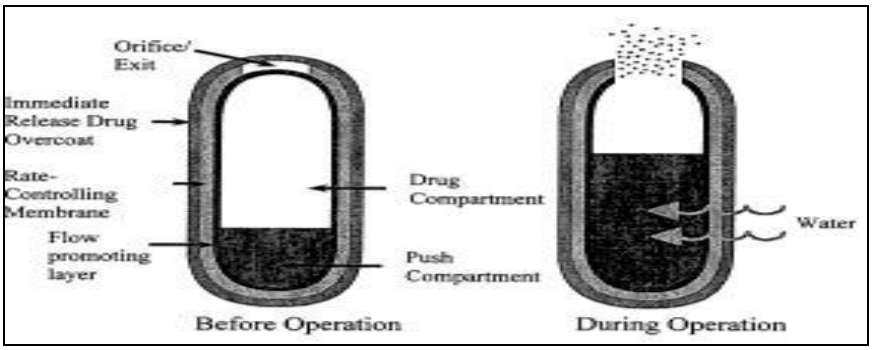

Fig.2- OROS Push-Stick Technology

4) Osmotic bursting osmotic pump[21]

Composition- Similar to an **Elementary osmotic pump** expect delivery orifice is absent and size may be smaller.

Mechanism of Action- When it is placed in an aqueous environment, water is imbibed and hydraulic pressure is built up inside until the wall rupture and the content are released to the environment.

Advantages- This system is useful to provide pulsated release.

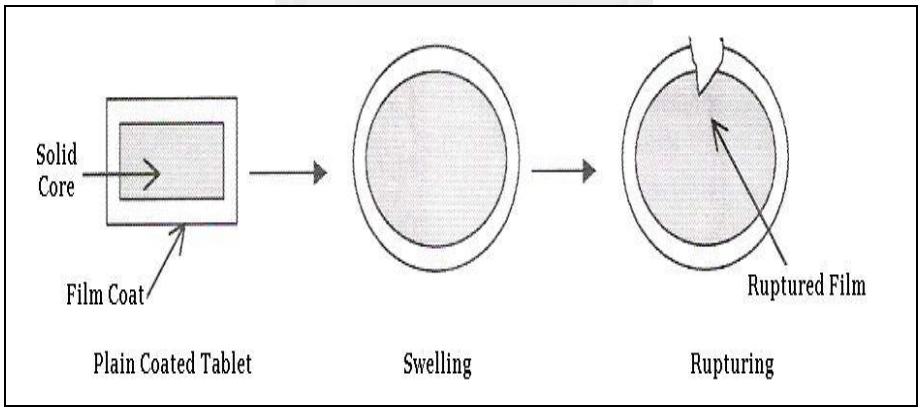

Fig.3-Osmotic bursting osmotic pump

5) Modified Osmotic Pumps

a) Controlled porosity osmotic pumps (CPOP)[22.23]

Composition- CPOPs are similar to EOP, the only difference being that the delivery orifice from which the drug release takes place is formed by incorporation of a water-soluble additive in the coating.

Mechanism of Action- After coming in contact with water, water soluble additives present in the coating dissolves and it results in an in situ formation of a microporous membrane as shown in figure. The release of drug takes place through this microporous channels as shown in figure.

Advantages- Eliminates the need for a separate manufacturing step (creating an orifice using a laser drilling machine).

Suitable for delivery of drugs having intermediate water solubility and extremes of water solubility by some modifications.

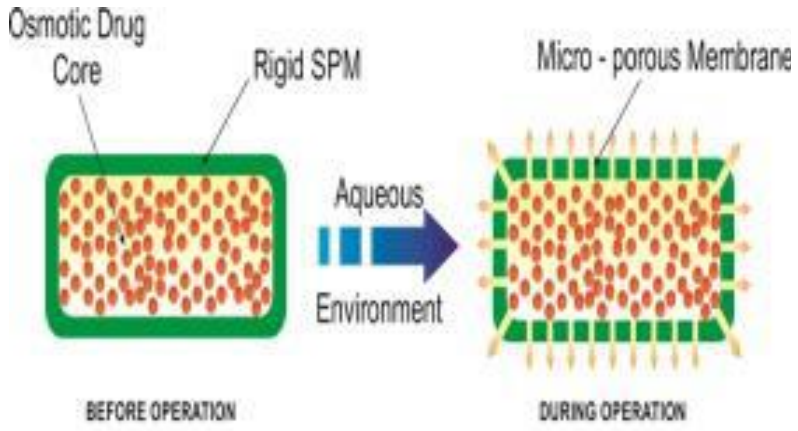

Fig.4- Controlled porosity osmotic pumps

6) Telescopic capsule for delayed release[24]

Composition- This device consists of two chambers, the first contains the drug and an exit port, and the second contains osmotic engine. Layer of wax-like material separates the two sections.

Mechanism of Action- As fluid is imbibed the housing of the dispensing device, the osmotic engine expand and exerts pressure on the slidable connected first and second wall sections.

7) Sandwiched osmotic tablet (SOTS)[25]

Composition- Tablet core consisting of a middle push layer and two attached drug layers is coated with a semipermeable membrane (SPM).

Mechanism of Action- After coming in contact with the aqueous environment, the middle push layer containing swelling agent swells and the drug is released from the delivery orifices.

Advantages- System delivers drug from two opposite orifices, rather from the single orifice of the **Push**-pull osmotic pump (PPOP).

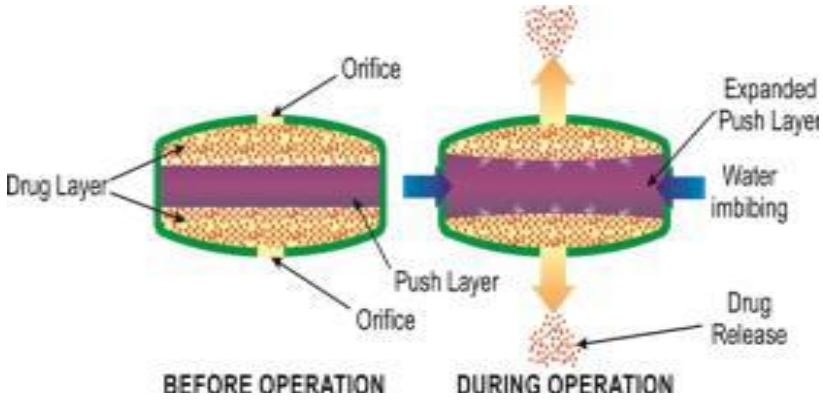

Fig.5- Sandwiched osmotic tablet

8) Liquid OROS controlled release system (L-OROS)

a) *Liquid OROS Soft cap* [26]

Composition- In Soft cap, Liquid drug formulation is present in a soft gelatin capsule, which is surrounded with the barrier layer, the osmotic layer, and the release rate-controlling membrane.

b) Liquid OROS hard cap

Composition- In hard cap, it consists of a liquid drug layer and an osmotic engine, all encased in a hard gelatin capsule and coated with semipermeable membrane.

Mechanism of Action- The expansion of the osmotic layer results in the development of hydrostatic pressure, thereby forcing the liquid formulation to break through the hydrated gelatin capsule shell at the delivery orifice.

Water is imbibed across the SPM, expanding the osmotic engine, which pushes against the barrier, releasing the drug through the delivery orifice.

Advantages -To deliver APIs as liquid formulations and combine the benefits of extended release with high bioavailability. Suitable for controlled delivery of lipophilic APIs

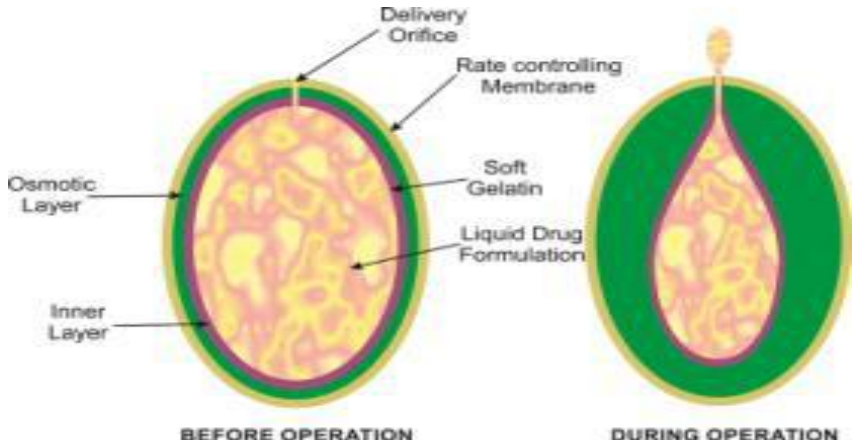

Fig.6- Liquid OROS Soft cap

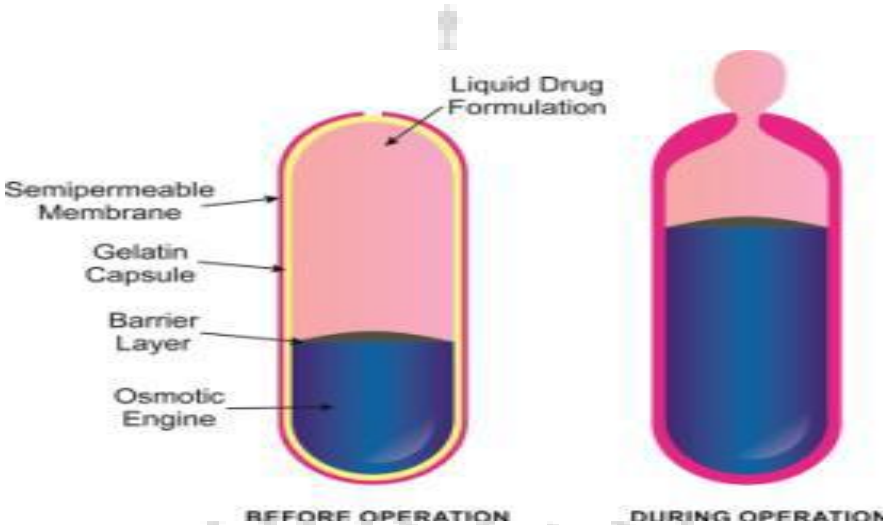

Fig.7- Liquid OROS hard cap

9) Multiple Chambers Osmotic Pumps

a) Push-pull osmotic pump (PPOP) [27]

Composition- Two compartments: Upper compartment (drug compartment) contains the drug along with osmotically active agents.

Lower compartment (push compartment) contains the polymeric osmotic agents.

Mechanism of Action- When the dosage form comes in contact with the aqueous environment, both compartments imbibe water simultaneously. Because the lower compartment is devoid of any orifice, it expands and pushes the diaphragm into the upper drug chamber, thereby delivering the drug via the delivery orifice.

Advantages- Deliver both highly water-soluble (oxybutynin hydrochloride) and practically water-insoluble (nifedipine, glipizide) drugs.

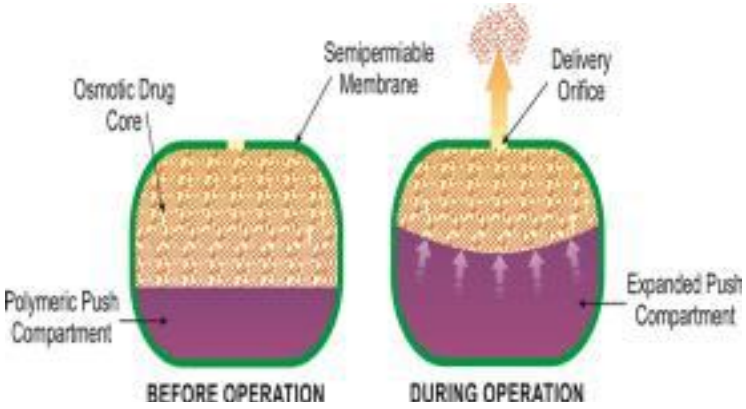

Fig.8- Push-pull osmotic pump (PPOP)

EVALUATION

- ✓ HARDNESS
- ✓ DISSOLUTION
- ✓ WEIGHT VARIATION
- ✓ PORE DIAMETER
- ✓ FRIABILITY
- ✓ COATING THICKNESS
- ✓ IN VITRO EVALUATION
- ✓ IN VIVO EVALUATION

Table No. 1. MARKET PRODUCTS

BRAND NAME	SALT	USED
Sudafed® 24 Hour	pseudoephedrine	nasal decongestant
Ditropan XL	oxybutynin chloride	Overactive bladder. Symptoms of urge urinary incontinence, urgency and frequency
Alpress™ LP	prazosin	For the treatment of hypertension
Volmax	albuterol	bronchospasm in patients with reversible obstructive airway disease

CONCLUSION

The therapeutic value of a pharmaceutical product depends on own parts; the rate profile of drug absorption and the pharmacodynamics of the drugs. While formulating drug delivery system our main aim is to achieve therapeutic object i.e. to cure the disease in shortest period of time with least amount of drug with or without side effect. Osmotic pumps have excellence control on the drug delivery so these are mostly used now a day to achieve therapeutic objective.

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