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OSMOTIC PUMP DRUG DELIVERY-A NOVEL APPROACH

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ABSTRACT

Osmotic drug delivery system (ODDS) utilizes the basic principle of osmotic pressure for controlled release of drugs. It provides the release of drugs in controlled manner to maintain drug concentration within therapeutic window and minimizing toxic effects. ODDS delivers a drug to large extent is independent of the physiological factors of the gastrointestinal tract, pH etc. That is why it can be utilized for systemic as well as targeted delivery of drugs. The drug release from osmotic system controls the drug release by controlling various formulation factors such as solubility, osmotic pressure of the core components, size of the delivery orifice and nature of the rate controlling membrane. The design of osmotic system is achieved by optimizing formulation and processing factors to deliver drugs in preprogrammed rate and controlled manner. The present study explains about an update on osmosis, different types of osmotic systems, components of ODDS, key parameter sand some patents.

KEYWORDS: Osmotic drug delivery system, pH, Osmotic pressure.

❖ INTRODUCTION

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. 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.[1]

$$\Pi = Ø\ c\ RT$$

Where, Ø = Osmotic pressure,
Π = osmotic coefficient,
c = molar concentration,
R = gas constant,
T = Absolute temperature

❖ DEFINATIONS

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

Osmosis refers the process of spontaneous movement of a solvent from a solution of lower solute concentration to a solution of higher solute concentration through an ideal semi permeable membrane which is permeable only to the solvent but impermeable to solute. It is driven by a difference in solute concentrations across the membrane that allows passage of water, but rejects most solute molecules or ions. Osmosis is the phenomenon that makes osmotic controlled drug delivery in a reality. Osmotic pressure is the pressure applied to the higher concentrated solution side to prevent transport of water across the semi permeable membrane.

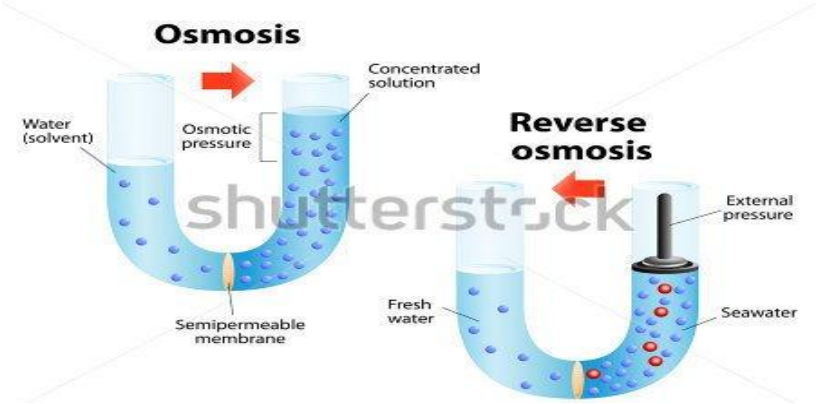

Fig.no: 1. Process of osmosis

Osmotic pressure is created due to imbibitions of fluid from external environment into the dosage form regulates the delivery of drug from osmotic devices. Rate of drug delivery from osmotic system is directly proportional to the osmotic pressure developed due to imbibitions of fluids by osmogen. Osmotic pressure is a colligative property of a solution where magnitude of osmotic pressure of the solution is independent on the number of discrete entities.[2]

❖ ADVANTAGES OF OSMOTIC DRUG DELIVERY SYSTEM

- Decrease frequency of dosing.
- Reduce the rate of rise of drug concentration in the body.
- Delivery may be pulsed or desired if required.
- Delivery ratio is independent of pH of the environment.
- Improve patient compliance.
- Reduce side effect.
- The delivery rate of zero-order is achievable with osmotic systems.
- A high degree of in IVIVC is obtained in osmotic system.
- Drug release is higher than conventional drug delivery system.
- Release rate of osmotic systems is highly predictable and can be programmed by modulating the release control parameters.

❖ DISADVANTAGES OF OSMOTIC DRUG DELIVERY SYSTEM

- Expensive
- Chance of toxicity due to dose dumping
- Rapid development of tolerance
- Hypersensitivity reaction may occur
- Integrity and consistency are difficult
- Release of drug depends on:
- size of hall
- surface area
- thickness and composition of membrane.[3]

❖ LIMITATION

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.[1]

❖ BASIC COMPONENTS OF OSMOTIC SYSTEMS

➢ DrugW

Which have short biological half-life and which is used for prolonged treatment are ideal candidate for osmotic systems. Various drug candidates such as Diltiazem HCl51, Carbamazepine, Metoprolol52, Oxprenolol, Nifedipine53, Glipizide54, etc are formulated as Osmotic delivery.[4]

➢ Osmotic agent

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
Lactose +Dextrose
Mannitol +Fructose
Mannitol +Dextrose
Dextrose +Sucrose
Mannitol +Sucrose[1]

➢ **Semipermeable Membrane**
An important part of the osmotic drug delivery system is the SPM housing. Therefore, the polymeric membrane selection is key to osmotic delivery formulation. The membrane must possess certain performance criteria 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. e.g. Cellulose esters like cellulose acetate, cellulose acetate butyrate, cellulose triacetate and ethyl cellulose and Eudragits.[4]

➢ **Wicking agent**
A wicking agent is defined as a material with the ability to draw water into the 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 physisorption with water. Physisorption is a formof absorption in which the solvent molecules can loosely adhere to surfaces of the wicking agent via Vander Waals interactions between the surface of the wicking agent and the adsorbed molecule. The function of the wicking agent is to carry water to surfaces inside the core of the tablet, thereby 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 molecular weight poly vinyl pyrrolidone (PVP), m-pyrol, bentonite, magnesium aluminium silicate, polyester and polyethylene.[5]

➢ **Pore forming agent**
These agents are particularly used in the pumps developed for poorly water soluble drug and in the development of controlled porosity or multiparticulate osmotic pumps. These poreforming agents cause the formation of microporous membrane. The microporous 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, mannitol and, diols and polyols such as poly hyric alcohols and polyvinyl pyrrolidone can be used as pore forming agents.[5]

➢ **Coating solvent**
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), acetoneethanol (80:20), acetone-water (90:10), methylene chloride-methanol (79:21), methylene chloride-methanol-water (75:22:3) etc. can be used.[5]

➢ **Plasticizers**
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 behavior of polymers and these changes may affect the permeability of the polymeric films.
Some of the plasticizers used are as below:
1. Polyethylene glycols
2. Ethylene glycol monoacetate; and
3. diacetate- for low permeability
4. Tri ethyl citrate
5. Diethyl tartarate or Diacetin- for more permeable films.[5]

❖ **CLASSIFICATION OF OSMOTIC DRUG DELIVERY SYSTEM**
Many forms of osmotic pumps are reported in the literature but in general they can be divided in implantable and oral systems.

A. IMPLANTABLE OSMOTIC PUMP
1. Rose and Nelson Pump
In the year 1955, these two Australian physiologists reported the first osmotic pump to the gut of sheep and other cattle. The pump is constructed of three chambers viz., a drug chamber with an orifice, a salt chamber with elastic diaphragm containing excess solid salt, and a water chamber. A semipermeable membrane separates the drug and water chamber. The difference in osmotic pressure across the membrane moves water from the water chamber into the salt. The volume of chamber increases because of this water flow, which distends the latex diaphragm separating the salt and drug chambers, there by pumping drug out of the device.[6]

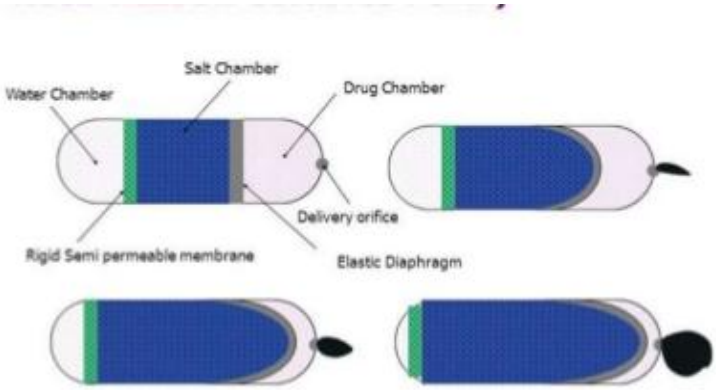

Fig. no. 2. Rose and Nelson osmotic pump

2. Higuchi- Theeuwes Pumpw

In the early 1970 Higuchi-Theeuwes developed a similar form of Rose-Nelson pump as shown in the figure. The semipermeable wall itself acts as a rigid outer casing of the pump. The device is loaded with drug prior to use. When the device is put in an aqueous environment the release of the drug follows a time course set by the salt used in the salt chamber and the permeability of the outer membrane casing. Ehp[23yj`rt ehp[6]

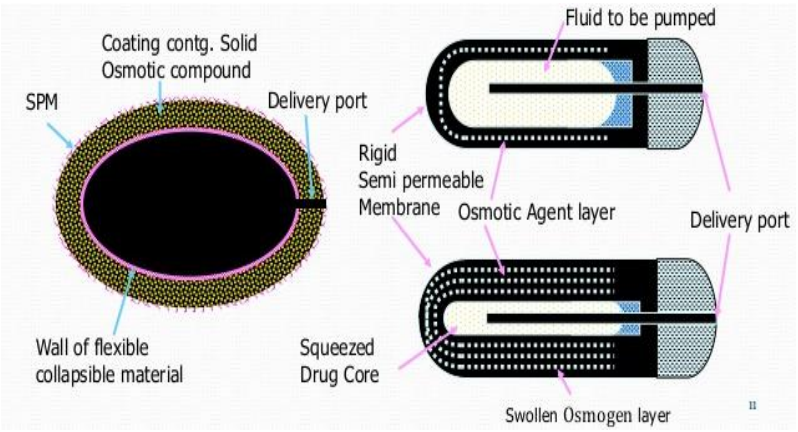

Fig.no.3. Higuchi- Theeuwes Pump

3. Higuchi-Leeper Pump

The Higuchi-Leeper pump is modified version of Rose-Nelson Pump. It has no water chamber, and the device is activated by water imbibed from the surrounding environment. The pump is activated when it is swallowed or implanted in the body. This pump consists of a rigid housing, and the semipermeable membrane is supported on a perforated frame. It has a salt chamber containing a fluid solution with excess solid salt. Recent modification in Higuchi-Leeper pump accommodated pulsatile drug delivery. The pulsatile release was achieved be the production of a critical pressure at which the delivery orifice opens and releases the drug.[6]

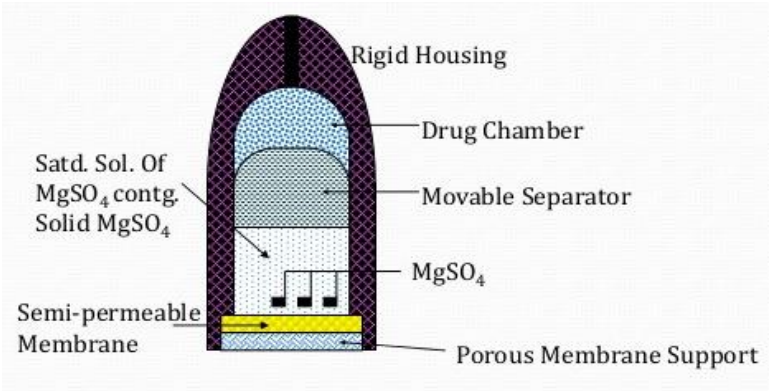

Fig. no. 4. Higuchi-Leeper Pump

Implantable miniosmotic pump

They are may be used in experimental animals or in human being.

1. DUROS® technology

DUROS technology, as shown in figure, provides a bicompartment system separated by a piston. One of the compartments consists of osmotic engine specifically formulated with an excess of solid NaCl, such that it remains present throughout the delivery period and results in a constant osmotic gradient. It also consists of a semi permeable membrane on one end through which water is drawn into the osmotic engine and establishes a large and constant osmotic gradient between the tissue water and the osmotic engine. Other compartment consists of a drug solution with an orifice from which the drug is released due to the osmotic gradient. This helps to provide site specific and systemic drug delivery when implanted in humans. The preferred site of implantation is subcutaneous placement in the inside of the upper arm. The delivery period ranges from some days to 1 year.

Materials used in this technology are screened for compatibility and the suitable and biocompatible ones are used. Radiation sterilization (gamma) was utilized to sterilize the final drug product. If the drug formulation cannot withstand sterilizing doses of radiation, then a DUROS subassembly is radiation sterilized and the drug formulation is added in a final aseptic operation. Hence, the materials of the system were also screened for their ability to withstand sterilizing doses of radiation.

This technology has the potential to provide more flexibility than competitive products regarding the types of drugs that can be administered, including proteins, peptides and genes because the drug dispensing mechanism is independent from the drug substance[2,6]

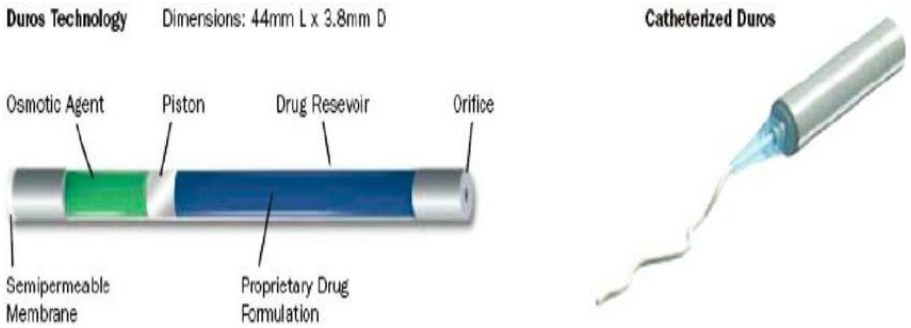

Fig. no. 5. DUROS Technology

2. ALZET miniosmotic Pumps

ALZET osmotic pumps, as shown in Figure**,** are miniature, implantable pumps used for research in animals like mice, rats etc. These infusion pumps continuously deliver drugs, hormones and other test agents at controlled rates from one day to six weeks without the need for external connections or frequent handling which eliminates the need for repeated night time or weekend dosing. ALZET pumps can be used for systemic administration for targeted drug delivery when implanted subcutaneously or intraperitoneally. They can be attached to a catheter for localization of the effect of the drug and for intravenous, intracerebral, or intra-arterial infusion to deliver hundreds of different compounds, including antibodies, chemotherapeutic drugs, cytokines, growth factors, hormones, and peptides.

ALZET pumps operate by osmotic displacement. An empty reservoir within the core of the pump is filled with the drug or hormone solution to be delivered, which is isolated from the chamber containing salt by a semi permeable membrane. Due to the presence of a high concentration of salt in a chamber surrounding the reservoir, water enters the pump through the semi permeable layer. The entry of water increases the volume in the salt chamber, causing compression of the flexible reservoir and delivery of the drug solution into the animal via the exit port. [2,6]

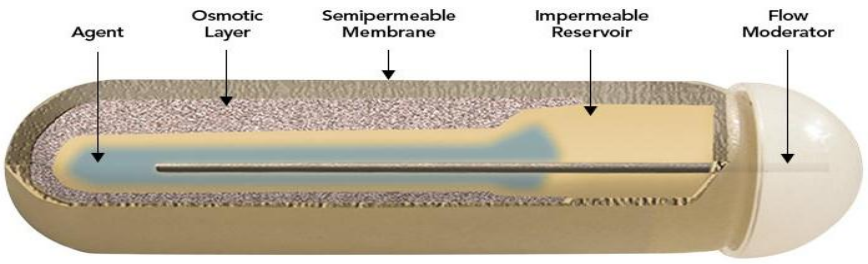

Fig. no. 6. ALZET osmotic pump

3. LiRIS®

It is a small and flexible single compartment osmotic system that can move freely in human bladder. It is introduced by Lee and Cima from Massachusetts Institute of Technology. The LiRIS® Lidocaine Releasing Intravesical System is used for the treatment of interstitial cystitis and painful bladder syndrome(IC/PBS).The device is based on a double lumen medical grade PDMS tube. One part of lumen is incorporated with lidocaine tablets whrereas the other part incorporates a shape memory wire made of nitinol.By nonsurgical procedures (catheter or cytoscopy) the device is inserted as well as retrieved from the bladder. Interstices breaks between the lidocaine tablets together with the super elastic effect of the wire allow the deformation of the system into a linear shape for insertion and return to its pretzel like post insertion. After insertion of the device into the bladder the whole silicone tube operates as the semi permeable membrane and a small laser drilled orifice within its wall acts as the lidocaine release outlet.[2]

Ivomec SR®Bolus

The pump is introduced by Merck &Co Inc,NJ,USA having a diameter of 20 to 30mm and length of about 100mm.It is generally used for veterinary purpose. It is designed to administer ivermectin directly in the lumen of cattles.The device is sedimented in the lumen of the animal due to its higher density(upto 3g/cm3).The wax based piston separates the osmotic agent compartment and the drug compartment of the device. The thermoresponsive drug formulations melt at the body temperature of cattle and it is pushed out by the piston, using push meltTM technology. The steady state of the drug can be maintained for 135 days with the pump.[2]

2. ORAL OSMOTIC PUMP

1) Single Chamber Osmotic Pumps

a) Elementary Osmotic Pumps

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

Elementary osmotic pump is constructed by coating an osmotically active agent with the rate controlling SPM. This membrane contains an orifice of a critical size through which the drug is delivered. Drug release through this system occurs in a controlled pattern because of the water permeation characteristics of a semi permeable membrane surrounding drug and osmotic properties of the osmogen in the formulation. The dosage form after coming into contact with aqueous fluids, imbibes water from the surroundings at a rate determined by the fluid permeability of the membrane and osmotic pressure of the core formulation. This osmotic imbibitions of water result in formation of a saturated solution of drug within the core, which is dispensed at controlled rate from the delivery orifice in the membrane. Though 60 -80 percent of drug is released at a constant rate from the EOP, a lag time of 30-60 minute is observed in most of the cases as the system hydrates before zero order delivery from the system begins. This system is suitable or delivery of drugs having moderate water solubility.

Advantage

Suitable for delivery of drugs having moderate water solubility.[1,6]

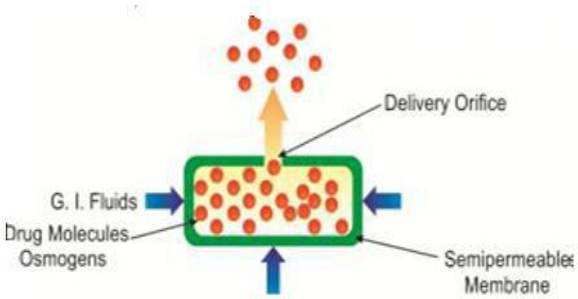

Fig. no. 7. Elementary Osmotic Pump

2. Multiple Chambers Osmotic Pumps

a) Push-pull osmotic pump (PPOP)

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

Push pull osmotic pump is a modified EOP which can be used for the delivery of both poorly water-soluble and highly water soluble drugs at a constant rate. This system resembles a standard bilayer tablet of which the upper layer contains drug and the lower layer, along with the tablet excipients, contains a polymeric osmotic agent which has the ability to form a suspension of drug in-situ. These layers are formed separately and bonded together to form a single bilayer core tablet which is further coated with a semi permeable membrane.

A small hole is then 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. The osmotic attraction in the drug layer pulls water into the compartment to form in situ a suspension of drug. The osmotic agent in the non-drug layer simultaneously attract water into that compartment, causing it to expand volumetrically and the expansion of non drug layer pushes the drug suspension out of the delivery orifice.

Advantages
Deliver both highly water-soluble (oxybutynin hydrochloride) and practically water-insoluble (nifedipine, glipizide) drugs.[1,6]

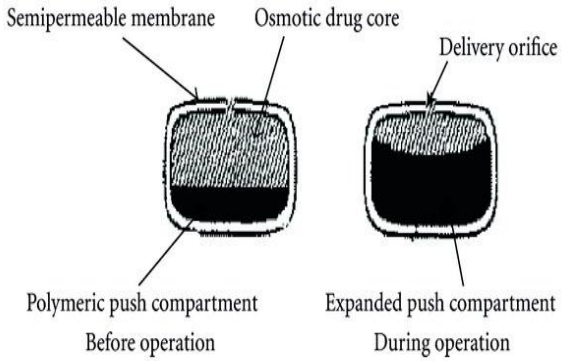

Fig. no. 8. Push-pull osmotic pump (PPOP)

b) Osmotic Pump with Non-Expanding Second Chamber
Composition-Multi-chamber devices comprise of systems containing a non-expanding second chamber.

Mechanism of Action
The second category of multi-chamber devices comprises system containing a non-expanding second chamber. This group can be divided into two sub groups, depending on the function of second chamber.

In the first device, this second chamber is used to dilute the drug solution which is released in the body because in certain cases where the drug is released in a concentrated form, it causes the problem of irritation in the gastrointestinal tract.

In the second device, there are two rigid chambers, wherein the first one contains a biologically inert osmotic agent, such as sugar or a simple salt like sodium chloride and the second chamber contains the drug. Water is drawn into both the chambers through the surrounding semi permeable membrane. The solution of osmotic agent formed in the first chamber then passes through the connecting hole to the drug chamber where it mixes with the drug solution before exiting through the micro porous membrane that form a part of wall surrounding the chamber. The device could be used to deliver relatively insoluble drugs.

Advantages- Relatively insoluble drugs can also be delivered.[1,6]

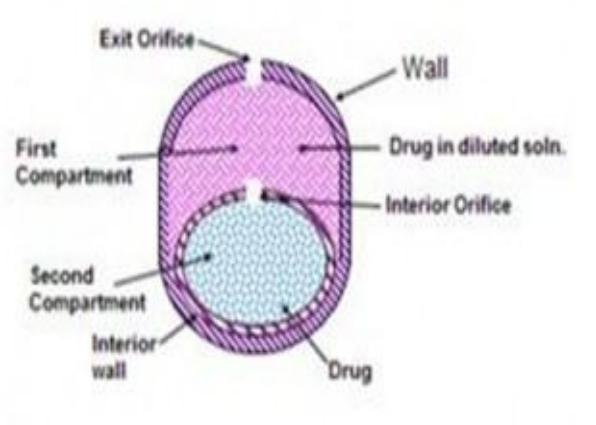

Fig. no. 9: Osmotic pump with non expanding second chamber

3. SPECIFIC TYPE
a) Bursting osmotic pump
b) Liquid oral osmotic system (L-OROS)
c) Multiparticulate Delayed Delivery Osmotic device
d) Telescopic capsule
e) Sandwiched osmotic tablet

a) Bursting Osmotic Pump
Composition Similar to an Elementary osmotic pump expect delivery orifice is absent and size may be smaller.

Mechanism of action
This system is similar to an EOP expect delivery orifice is either absent or size may be small. When it is placed in an aqueous environment, water is imbibed through the semipermeable membrane and hydraulic pressure is built up inside until the membrane ruptures and the content is released. Drug release can be modulated by varying the thickness and area of the semipermeable membrane. This system is useful to provide pulsated drug release .

Pulsatile delivery system
Pulsatile systems are gaining a lot of interest as they deliver the drug at the right site of action at the right time and in the right amount, thus providing spatial and temporal delivery and increasing patient compliance. These systems are designed according to the circadian rhythm of the body. The principle rationale for the use of pulsatile release is for the drugs where a constant drug release, i.e., a zero order release is not desired. The release of the drug as a pulse after a lag time has to be designed in such a way that a complete and rapid drug release follows the lag time. This type of tablet system consist of core coated with two layer of swelling and rupturable coatings herein they used spray dried lactose and microcrystalline cellulose in drug core and then core was coated with swelling polymer croscarmellose sodium and an outer rupturable layer of ethylcellulose. Pulsatile systems can be classified into single and multiple-unit systems.

Single-unit systems are formulated either as capsule-based or osmosis based systems. Single-unit systems are

designed by coating the system either with eroding/soluble or rupturable coating.

In multiple-unit systems, however, the pulsatile release is induced by changing membrane permeability or by coating with a rupturable membrane.

Advantages- This system is useful to provide pulsated release.[1.6]

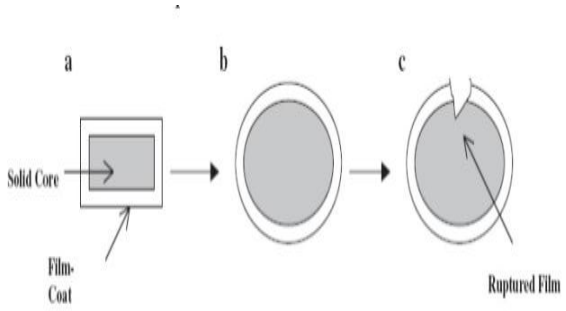

Fig. no. 10. Bursting osmotic pump

b) Liquid Oral Osmotic System

Liquid oral osmotic system (OROS) as shown in figure and is designed to deliver drugs as liquid formulations and combine the benefits of extended release with high bioavailability. They are of three types namely L- OROS hard cap, L- OROS soft cap and delayed liquid bolus delivery system.

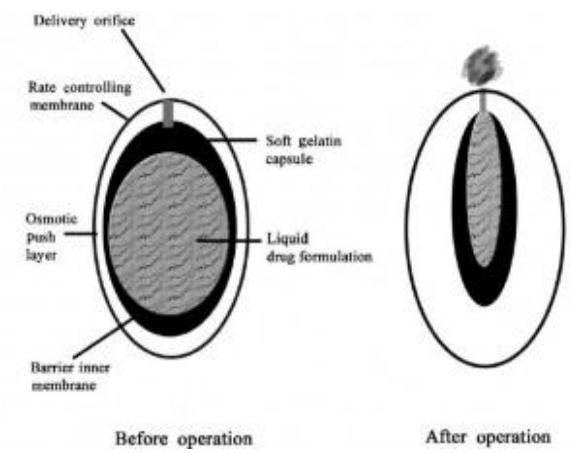

Fig. no: 11. L-OROS soft cap

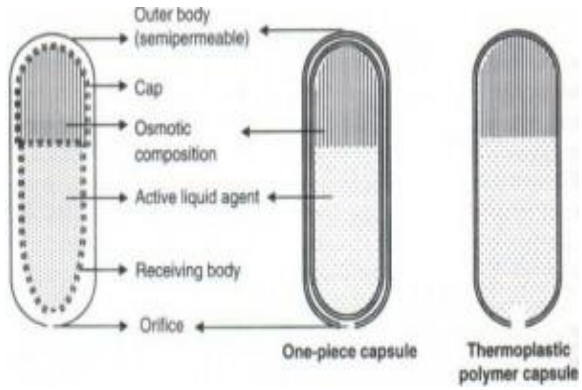

Fig. no.12. L-OROS hard cap

Each of these systems includes a liquid drug layer, an osmotic engine or push layer and a semi permeable membrane coating. When the system is in contact with the aqueous environment water permeates across the rate controlling membrane and activate the osmotic layer. The expansion of the osmotic layer results in the development of hydrostatic pressure inside the system, thereby forcing the liquid formulation to be delivered from the delivery orifice. L-OROS hardcap and softcap systems are designed to provide a continuous drug delivery while L-OROS delayed liquid bolus drug delivery system is designed for pulsatile drug delivery. The delayed liquid bolus delivery system comprises three layers: a placebo delay layer, a liquid drug layer and an osmotic engine, all surrounded by rate controlling semi permeable membrane.

The delivery orifice is drilled on the placebo layer end of the capsule shaped device. When the osmotic engine is expands, the placebo is released first, delaying release of the drug layer. Drug release can be delayed from up to 10 hours, depending on the permeability of the rate controlling membrane and thickness of the placebo layer.[7]

c. Multiparticulate Delayed-Release osmotic system

In the multiparticulate delayed-release system pellets containing drug with or without osmotic agent are coated with an SPM-like cellulose acetate. On contact with an aqueous environment, water penetrates into the core and forms a saturated solution of soluble components. The osmotic pressure gradient induces a water influx, resulting in a rapid expansion of the membrane, leading to the formation of pores. The osmotic ingredient and the drug are released through these pores according to zero order kinetics. In a study by Schultz and Kleinebudde[37], lag time and dissolution rates were found to be dependent on the coating level and osmotic properties of the dissolution medium. Furthermore, dissolution characteristics were found to be influenced by such membrane components as incorporation of plasticizer and its concentration and lipophilicity. Because of their semi permeable walls, an osmotic device inherently show lag time before drug delivery begins. Although this characteristic is usually cited as a disadvantage, it can be used advantageously. The delayed release of certain drug (drugs for early morning asthma or arthritis) may be beneficial.[24]

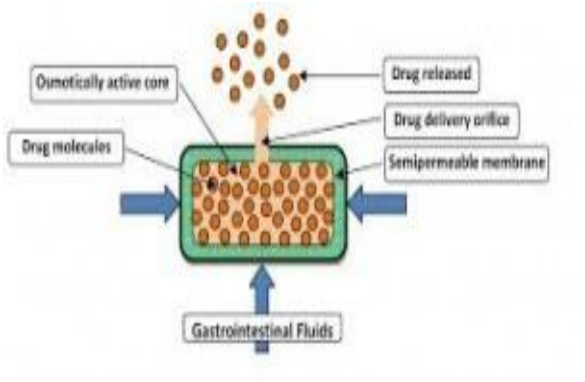

Fig.no: 13 Multiparticulate delayed release system

d. Telescopic Capsule for Delayed Release

A bilayer osmotic tablet is prepared, whose one of the chambers contains a drug with an orifice and other chamber contains an osmotic engine. The filling of the drug is either performed manually or by an automated filling machine. These two layers are separted by a waxy material. This tablet is fitted inside a capsule in such a way that the osmotic layer faces towards the completed end of the cap and the drug with the exit port faces towards the open end of the cap.

The cap, bilayer tablet and the body are fitted together tightly. As the water is imbibed in the housing of the dispensing device, the osmotic engine expands and exerts pressure on the slidable walls of the bilayer tablet and the capsule. A negligible pressure gradient between the external environment and the interior of the system is developed as a result of which there is a minimal net flow of environmental water. Consequently, no agent is delivered for this delayed period of time.[25] A schematic diagram is seen in the figure-

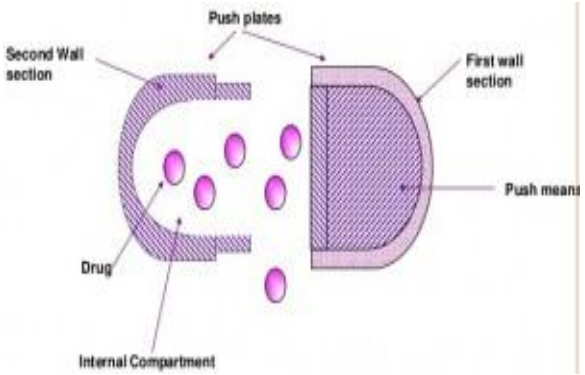

Fig. no: 14. Telescopic capsule for delayed release

e. Sandwiched osmotic tablet (SOTS)

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).[22]

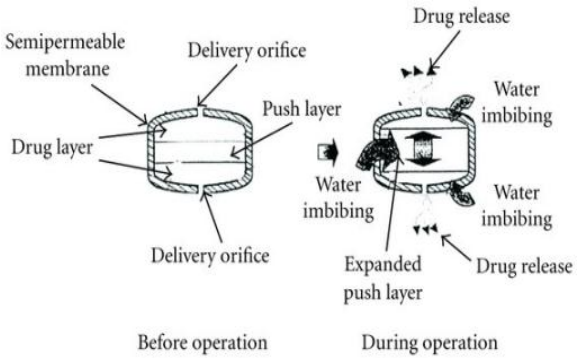

Fig. no.15. Sandwiched osmotic tablet

EVALUATION

A) Weight variation
B) Hardness
C) Friability
D) Thickness
E) Pore diameter
F) Coating thickness
G) In vitro evaluation

It has been evaluated by the conventional USP paddle and basket type apparatus. The dissolution medium is distilled water as well as simulated gastric fluid (for first 2-4 h) have been used.

H) In vivo evaluation

It has been carried out mostly in dogs. As the environment in the intestinal tract of the dog is very similar to that of human beings terms of both pH and motility, dogs have been used widely for in vivo delivery rate measurement of drugs from osmotically controlled oral drug delivery systems and also to establish in vitro in vivo correlation.

Monkeys can also be used but in most of the studies the dogs are preferred.

MARKETED PRODUCT

Elementary Osmotic Pump

Brand Name	API
Efidac 24 ®	Chlorpheniramine
Acutrim ®	Phenylpropanolamine
Sudafed 24 ®	Pseudoephedine
Volmax ®	Albuterol

Push-Pull Osmotic Systems

Brand Name	API
Ditropan XL ®	Oxybutynin chloride
Procardia XL®	Nifedipine
Glucotrol ®	Glipizide
DynaCirc CR®	Isradipine56
Invega®	Paliperidone57

Implantable Osmotic Systems

Brand Name	API
Viadur®	Leuprolide acetate
Chronogesic™	Sufentanil

❖ CONCLUSION

In osmotic delivery systems, osmotic pressure provides the driving force for drug release. Increasing pressure inside the dosage form from water incursion causes the drug to release from the system. The major advantages include precise control of zero-order or other patterned release over an extended time period—consistent release rates can be achieved irrespective of the environmental factors at the delivery site. Controlled delivery via osmotic systems also may reduce the side-effect profile by moderating the blood plasma peaks typical of conventional (e.g., instant release) dosage forms. Moreover, since efficacious plasma levels are maintained longer in osmotic systems, avoidance of trough plasma levels over the dosing interval is possible.

However, a complex manufacturing process and higher cost compared with conventional dosage forms limit their use. Although not all drugs available for treating different diseases require such precise release rates, once-daily formulations based on osmotic principles are playing an increasingly important role in improving patient compliance. Therefore, most of the currently marketed products are based on drugs used in long-term therapies for diabetes, hypertension, attention-deficit disorder, and other chronic disease states. Besides oral osmotic delivery systems, implants that work on osmotic principles are promising for delivery of a wide variety of molecules with a precise rate over a long period of time. Further, with the discovery of newer and potent drugs by the biotechnology industry, the need to deliver such compounds at a precise rate certainly will pave the way for osmotic delivery systems to play an increasingly important role in drug delivery.

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