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OSMOTIC DRUG DELIVERY SYSTEM: A PROMISING DRUG DELIVERY TECHNOLOGY

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ABSTRACT

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 utilize osmotic pressure for controlled delivery of active agent(s). The release of drug(s) from osmotic systems is independent of gastric pH and gastric motility. 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 preferably focuses on all types of ODDS, formulation of ODDS, factors affecting release of drug and various formulation factors affecting the systems.

KEYWORDS

Osmosis, Osmotic drug delivery systems, Zero order release and Formulation factors.

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INTRODUCTION[1-10]

The first report of an osmotic effect dates to Abbenollet {1748}. But Pfeffer obtained the first quantitative measurement in 1877. 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 upto 10 -16 hrs). **Osmolality** is the number of osmoles per Kg of water. **Osmolarity** is the number of osmoles per liter

of solution. **So-osmotic** solution is one where two solution are separated by a perfect semi permeable membrane (SPM is membrane which is permeable only to solvent molecule and no net movement of solute occur across the membrane Osmotic pressure is a most important colligative property according to Pharma point of view. Colligative property is the concentration of solution independent of solute property. Osmotic pressure of a solution is the external pressure that must be applied to the solution in order to prevent it being diluted by the entry of solvent via a process known as Osmosis.

Need for Developing Odds

1. In order to reduce the dose.
2. To decreases dose related side effect**.**
3. To minimizes rate of administration.
4. To provide controlled release and
5. To increase patient compliance.

Mechanism of osmosis

Core contain water soluble osmotically active agent and blended with water soluble or insoluble drug, additives and coating has been carried out which functions as semi permeable membrane. Since barrier is only permeable to water, initial penetration of water dissolves the critical part of the core, resulting in development of an osmotic pressure difference across the membrane. The device delivers a saturated volume equal to the volume of water uptake through the membrane. Initial lag time (per hour) during which delivery rate increases to its maximum value, drug release is zero order, until all solid material is dissolved.

The relation between Osmotic pressure (n) and the concentration of non-electrolyte is given for dilute solution which may be assumed to exhibit ideal behavior by the Van't Hoff equation,

$$nv = n^2RT$$

Where, V = is the volume of solution.

n^2 = is number of moles of solute.

T = thermodynamic temperature and

R = is the gas constant.

Advantages of Osmotic Drug Delivery Systems

1. The delivery rate of zero-order is achievable with osmotic systems.
2. Delivery may be delayed or pulsed, if desired.
3. Higher release rates are possible with osmotic systems compared with conventional diffusion-controlled drug delivery systems.
4. The release rate of osmotic systems is highly predictable and can be programmed by modulating the release control parameters.
5. For oral osmotic systems, drug release is independent of gastric pH and hydrodynamic conditions.
6. The release from osmotic systems is minimally affected by the presence of food in gastrointestinal tract.
7. A high degree of in vivo- in vitro correlation (IVIVC) is obtained in osmotic systems.

Limitations of Osmotic Drug Delivery Systems

1. Special equipment is required for making an orifice in the system.
2. Residence time of the system in the body varies with the gastric motility and food intake.
3. It may cause irritation or ulcer due to release of saturated solution of drug**.**

Formulation of Osmotic DDS

The Core is made up of Active Drug, Filler, and Viscosity modifier, Solubilizer, Lubricant or Glidant. While coating composed of Polymer, Plasticizer, Membrane modifier, Color and Opacifier.

Drug

Drug itself may act as an osmogen and shows good aqueous solubility (e.g., potassium chloride pumps). But if the drug does not possess an osmogenic property, osmogenic salt and other sugars can be incorporated in the formulation.

Semipermeable Membrane

Semipermeable membrane must possess certain performance criteria:

- It must have sufficient wet strength and water permeability.
- It should be selectively permeable to water and biocompatible.
- Some other polymers such as agar acetate, amylose triacetate, betaglucan acetate, poly (vinylmethyl) ether copolymers, poly (orthoesters), poly acetals, poly (glycolic acid) and poly (lactic acid) derivatives.

- The unique feature of Semipermeable membrane utilized for an osmotic pump is that it permits only the passage of water into the unit, thereby effectively isolating the dissolution process from the gut environment.

Osmogen or Osmagent or Osmotic Driving Agent

Osmotic agents are classified into organic and inorganic polymeric agents like Na-cmc and magnesium sulphate etc.

Hydrophilic and Hydrobhobic Polymers

These polymers are used in the formulation development of osmotic systems containing matrix core. The selection of polymer is based on the solubility of drug as well as the amount and rate of drug to be released from the pump. The highly water soluble compounds can be co-entrapped in hydrophobic matrices and moderately water soluble compounds can be co-entrapped in hydrophilic matrices to obtain more controlled release. Examples of hydrophilic polymers are hydroxy ethyl cellulose, carboxy methyl cellulose, hydroxyl propyl methyl cellulose, etc. Examples of hydrophobic polymers are ethyl cellulose, wax materials, etc.

Wicking agents

It is defined as a material with the ability to draw water into the porous network of a delivery device. The function of the wicking agent is to draw water to surfaces inside the core of the tablet, thereby creating channels or a network of increased surface area. Examples are colloidon silicon dioxide, kaolin, titanium dioxide, alumina, niacinamide, sodium lauryl sulphate (SLS), low molecular weight polyvinyl pyrrolidone (PVP), bentonite, magnesium aluminium silicate, polyester and polyethylene, etc.

Solubilizing Agents

Non swellable solubilizing agents are classified into three groups

1. Agents that inhibits crystal formation of the drugs or otherwise act by complexation of drug (e.g., PVP, PEG, and Cyclodextrins).
2. A high HLB micelle forming surfactant, particularly anionic surfactants (e.g., Tween 20, 60, 80, poly oxy ethylene or polyethylene containing surfactants and other long chain anionic surfactants such as SLS).
3. Citrate esters and their combinations with anionic surfactants (e.g., alkyl esters particularly triethyl citrate).

Surfactants

They are added to wall forming agents. They act by regulating the surface energy of materials to improve their blending in to the composite and maintain their integrity in the environment of use during the drug release period. Examples: polyoxyethylenated glycerylrecinoleate, polyoxyethylenated castor oil having ethylene oxide, glyceryllaurates, etc.

Coating Solvents

Solvents suitable for making polymeric solution that is used for manufacturing the wall of the osmotic device include inert inorganic and organic solvents. Examples: methylene chloride, acetone, methanol, ethanol, isopropyl alcohol, ethyl acetate, cyclohexane, etc.

Plasticizers

Permeability of membranes can be increased by adding plasticizer, which increases the water diffusion coefficient. Examples: dialkyl phthalates, trioctyl phosphates, alkyl adipates, triethyl citrate and other citrates, propionates, glycolates, glycerolates, myristates, benzoates, sulphonamides and halogenated phenyls.

Flux Regulators

Flux regulating agents or flux enhancing agent or flux decreasing agent are added to the wall forming material; it assist in regulating the fluid permeability through membrane. Poly hydric alcohols such as poly alkylene glycols and low molecular weight glycols such as poly propylene, poly butylene and poly amylene, etc. can be added as flux regulators.

Pore Forming Agents

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. The pore formers can be inorganic or organic and solid or liquid in nature. Like,

- Alkaline metal salts such as sodium chloride, sodium bromide, potassium chloride, etc.
- Alkaline earth metals such as calcium chloride and calcium nitrate.

- Carbohydrates such as glucose, fructose, mannose, etc.

Factors Affecting Release of Medicament

Solubility

Solubility of drug is one of the most important factors since kinetic of osmotic release is directly related to the drug solubility. The fraction of a drug release with zero order kinetic is given by

$$F(z) = 1 - S P$$

Where F (z) = fraction release by zero order

S = drug solubility in g / cm^3

P = density of core tablet.

Drug with density of unity and solubility less than 0.05 g / cm^3 would release greater than or equals to 95 % by zero order kinetics

Drug with density > 0.3 g / cm^3 solubility would demonstrate with higher release rate > 70 % by zero order.

Osmotic Pressure

Rate of drug release from an Osmotic system is directly proportional to Osmotic Pressure of the core formulation

dM /dt = A k n C / h

In order to achieve optimized and constant Osmotic Pressure in compartment Osmotic agent must be added to tablet. So varying the osmogen vary osmotic pressure and hence drug release. Osmogen are classified as inorganic and organic osmogens.

Delivery Orifice

Formation of orifice can take place by,

1. Laser
2. Micro drill
3. Modified punches
4. Controlled porosity osmotic pumps can be generated by in-situ formation of delivery orifice which has been described in US Patent. In case of Propranolol Hcl Oral Osmotic Tablet.
5. Tablet with orifice diameter of 200 - 800 urn showed zero order release and
6. The same with 1 mm orifice diameter showed abnormal release. So infact orifice diameter should be below Amax and should be greater than Amin.since in vivo drug tablet will swell and still minimize the bore. So uneven and unpredictable release will occur. For delivery containing Kcl, orifice should be between 75 to 275 microns in diameter.

Membrane Type

Drug release from osmotic system is largely independent of pH and agitational intensity of GIT. Examples are Cellulose Ester, Cellulose Triacetate, Cellulose Propionate, Cellulose Acetate Butyrate, Ester, Ethyl Cellulose and Eudragits. Among above Cellulose Acetate Butyrate is most commonly used since of its,

1. High water permeability.
2. Permeability can be adjusted by varying the degree of acetylation of polymer and also by increasing plasticizer concentration.
3. Flux enhancer and Superior drying property to thermolabile drugs.
4. Superior drying property so advantageous to thermolabile drugs.

Osmotic Drug Delivery Devices[7]

They fall in two categories (Figure No.1),

Implantable

a) The Rose and Nelson Pump
b) Alzet osmotic pump
c) Higuchi Leeper Pump
d) Higuchi Theeuwes pump.

Oral Osmotic Pump

a) Single chamber osmotic pump
b) Elementary osmotic pump.

Multi chamber osmotic pump

a) Push pull osmotic pump
b) Osmotic pump with non-expanding second chamber.

Specific types of osmotic pumps

a) Controlled porosity osmotic pump
b) Osmotic bursting osmotic pump
c) Liquid OROS
d) Delayed Delivery Osmoticdevice
e) Telescopic capsule
f) Orosct (colon targeting)
g) Sandwiched oral therapeutic system
h) Osmotic pump for insoluble drugs
i) Monolithic osmotic systems.

Implantable osmotic pump

This is most versions in the category of implantable pumps developed by Alza Corporation as shown in

fig it is composed of three concentric layers-the drug reservoir, the osmotic sleeves and the rate controlling semi permeable membrane. The additional component called flow moderator is inserted into the body of the osmotic (Figure No.2).

The inner most compartment of drug reservoir which is surrounded by an osmotic sleeve, a cylinder containing high concentration of osmotic agent. The osmotic sleeve is covered by a semi permeable membrane when the system is placed in aqueous environment water enters the sleeve through semi permeable membrane, compresses the flexible drug reservoir and displaces the drug solution through the flow moderator. These pumps are available with variety of delivery rates between 0.25 to 10ml per hour and delivery duration between one day and four weeks (Figure No.3).

The Rose Nelson Pump[1]

In, 1955, two Australian physiologists reported the first osmotic pump. They were interested in delivery of drug to the gut of sheep and cattle. The pump consisted of three chambers 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 in to the salt chamber. The volume of chamber increases because of this water flow, which distends the latex diaphragm separating the salt and drug chambers, thereby pumping drug out of the device.

Alzet osmotic pump[9]

ALZET pumps operate because of an osmotic pressure difference between a compartment within the pump, called the salt sleeve, and the tissue environment in which the pump is implanted. The high osmolality of the salt sleeve causes water to flux into the pump through a semi permeable membrane which forms the outer surface of the pump. As the water enters the salt sleeve, it compresses the flexible reservoir, displacing the test solution from the pump at a controlled, predetermined rate. Because the compressed reservoir cannot be refilled, thepumps are designed for single-use only (Figure No.4).

Higuchi osmotic pump[1]

Design of Higuchi Leeper pump described in Figure No.5 represents the first simplified version of Alzet pump. It contains rigid housing and the semi permeable membrane, which is supported on a perforated frame. Rigid housing divides in two chambers by a movable separator. The benefit over rose nelson pump is that it does not have water chamber. And the device is activated by water imbibed from the surrounding environment. This means the pump can be prepared loaded with drug and then stored for weeks and months prior to use.

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 by the production of a critical pressure at which the delivery orifice opens and releases the drug (Figure No.6).

Higuchi-Theeuwes Pump

Further simplified variant of Rose-Nelson pump was developed by Higuchi and Theeuwes. This pump comprises a rigid, rate controlling outer semipermeable membrane surrounding a solid layer of salt coated on the inside by an elastic diaphragm and on the outside by the membrane. In use, water is osmotically drawn by the salt chamber, forcing drug from the drug chamber (Figure No.7).

Oral Osmotic Pump

Elementary Osmotic Pump[10,11]

The elementary osmotic pump is a new delivery system for drugs (Figure No.8). It delivers the agent by an osmotic process at a controlled rate. Control resides in the:

a) Water permeation characteristics of a semi permeable membrane surrounding the formulating agent.

b) Osmotic properties of the formulation In its simplest embodiment the system is constructed by coating an osmotically active agent with the rate controlling semi permeable membrane. This membrane contains an orifice of critical size through which agent is delivered. The dosage form after coming into contact with aqueous fluids, imbibes water 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. These system are suitable or delivery of drugs having moderate water solubility.

Multi chamber osmotic pump

Push Pull Osmotic Pump[12,13]

Push pull osmotic pump is a modified EOP (Figure No.9). Through, which it is possible to deliver both poorly water-soluble and highly water soluble drugs at a constant rate. This system resembles a standard bilayer coated tablet. One layer (depict as the upper layer) contains drug in a formulation of polymeric, osmotic agent and other tablet excipients. This polymeric osmotic agent has the ability to form a suspension of drug in situ. When this tablet later imbibes water, the other layer contains osmotic and colouring agents, polymer and tablet excipients. These layers are formed and bonded together by tablet compression to form a single bilayer core. The tablet core is then coated with semi permeable membrane. After the coating has been applied, a small hole is drilled through the membrane by a laser or mechanical drill on the drug layer side of the tablet. When the system is placed in aqueous environment water is attracted into the tablet by an osmotic agent in both the layers. 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.

Osmotic Pump with Non Expanding Second Chamber[14]

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 one category of these devices, the second chamber is used to dilute the drug solution leaving the devices. This is useful because in some cases if the drug leaves the oral osmotic devices a saturated solution, irritation of GI tract is a risk.

Specific types of osmotic pump

Osmotic Brusting Osmotic Pump[15]

This system is similar to an EOP expect delivery orifice is absent and size may be smaller. 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. Varying the thickness as well as the area the semi permeable membrane can control release of drug. This system is useful to provide pulsated release.

Liquid Oral Osmotic System[16,17]

Liquid OROS are designed to deliver drugs as liquid formulations and combine the benefits of extended release with high bioavailability. They are of two types: a) L OROS hard cap b) L OROS soft cap (Figure No.10).

Delayed liquid bolus delivery system

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 activates 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. Whereas L OROS hard cap or

soft cap system is designed to provide continuous drug delivery, the L OROS delayed liquid bolus drug delivery system is designed to deliver a pulse of liquid drug. 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 I to 10 hour.

Delayed Delivery Osmotic Device[18,19]

Because of their semi permeable walls, an osmotic device inherently show lag time before drug delivery begins (Figure No.11). 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. The following text describes other means to further delay drug release.

Telescopic Capsule for Delayed Release

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

OROS-CT

OROS-CT is used as a once or twice a day formulation for targeted delivery of drugs to the colon (Figure No.12). The OROS-CT can be a single osmotic agent or it can be comprised of as many as five to six push pull osmotic unit filled in a hard gelatin capsule.

After coming in contact with the gastric fluids, gelatin capsule dissolved and the enteric coating prevents entry of fluids from stomach to the system as the system enters into the small intestine the enteric coating dissolves and water is imbibed into the core thereby causing the push compartment to swell. At the same time flow able gel is formed in the drug compartment, which is pushed out of the orifice at a rate, which is precisely controlled, by the rate of water transport across the semi permeable membrane.

Sandwiched Osmotic Tablets (SOTS)[20]

It is composed of polymeric push layer sandwiched between two drug layers with two delivery orifices. When placed in the aqueous environment the middle push layer containing the swelling agent's swells and the drug is released from the two orifices situated on opposite sides of the tablet and thus SOTS can be suitable for drugs prone to cause local irritation of the gastric mucosa (Figure No.13).

Monolithic Osmotic System[21]

It constitutes a simple dispersion of water-soluble agent in polymer matrix. When the system comes in contact in with the aqueous environment. Water imbibitions by the active agents takes place rupturing the polymer matrix capsule surrounding the drug, thus liberating it to the outside environment. Initially this process occurs at the outer environment of the polymeric matrix, but gradually proceeds towards the interior of the matrix in a serial fashion. However this system fails if more then 20 -30 volumes per liter of the active agents are incorporated in to the device as above this level, significant contribution from the simple leaching of the substance take place.

Osmat[22]

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

Controlled Porosity Osmotic Pump[23,24]

The pump can be made with single or multicompartment dosage form, in either form, the delivery system comprises a core with the drug surrounded by a membrane which has an asymmetric structure, i.e. comprises a thin dense skin layer supported by a porous substructure. The membrane is formed by phase inversion process controlled by the evaporation of a mixed solvent system. Membrane is permeable to water but impermeable to solute and insensitive pore forming additive dispersed throughout the wall. When exposed to water, low levels of water-soluble additive are leached from polymer materials that were permeable to water yet remained insoluble. Then resulting sponge like structure formed the controlled porosity walls of interest and was substantially permeable to both water and dissolved drug agents. Rate of drug delivery depends upon the factors are water permeability of the semi permeable membrane and the osmotic pressure of the core formulation, thickness and total surface area of coating.

Modified osmotic pump[25,26]

Osmotic pumps for moderately soluble drugs

Semi permeable membrane must be 200-300 microns thick to withstand the pressure generated within the device. These thick membranes lowers water permeation rate, which is not desirable for moderately soluble drugs. This problem can be overcome by using coating materials with high water permeability. For example, addition of plasticizers and water soluble additive to the cellulose acetate membranes, this increased the permeability of membrane up to tenfold. Composite structured semi permeable membrane is used for moderately soluble drugs. The first layer is made up of thick micro porous film that provides the strength required to withstand the internal pressure, while second layer is composed of thin semi permeable membrane that produces the osmotic flux. The support layer is formed by, Cellulose acetate coating containing 40 to 60% of pore forming agent such as Sorbitol (Figure No.14).

Osmotic Pump for Insoluble Drugs

Osmotic agents are coated with an elastic semi permeable membrane film in fluid bed coater and this particle are then mixed with insoluble drugs and compressed to form tablet which is coated with SPM and orifice is created in membrane. After coming in contact with aqueous environment, water is drawn through the two membranes into the osmotic agent particle which swells and hydrostatically pushes the insoluble drug via the orifice (Figure No.15).

Multichamber Osmotic Pump

Although EOP is simple to design and well suited for drug with intermediate water solubility there are many drugs with either poor or high water solubility. This problem has led to development of MOP. There are two type of MOP.

Expandable[27,28]

For Solid Osmotic System

PPOP (Push Pull Osmotic Pump), contain two compartment separated by elastic diaphragm means Bilayer or Trilayer. Upper compartment contain drug with or without osmogen (drug compartment nearly 60 - 80 %) and lower compartment (Push compartment) contain Osmogen at 20 - 40 %. Example Procardia XL for Nifedipine.

For Liquid Osmotic System

A liquid formulation is use for delivering insoluble drugs and macromolecules. Such molecules require external liquid components to assist in solubilization, dispersion, protection from enzymatic degradation and promotion of gastrointestinal absorption. Thus

the L-OROS system was designed for continuous delivery of liquid drug (Figure No.16).

Non Expandable

Non expandable osmotic pump maintains the volume throughout the period of operation means the rigid one. Depending on function of second chamber non-expandable osmotic pump are divided into two subtypes,

i) Drug solution gets diluted in second chamber before leaving device.

Such is useful when saturated solution of drug irritate GIT.

ii) Two separate EOP tablet formed in single tablet.

Here one chamber contains osmogen and second chamber contain drug. When such system comes in contact with aqueous environment, solution of osmotic agent formed in first chamber is delivered to drug chamber via the concentric hole, where it mixes with drug solution before coming out of the micro porous membrane that forms the pores of SPM surrounding the drug chamber useful for insoluble drug delivery (Figure No.17).

Controlled Porosity Osmotic Pump

It is laser or micro driven orifice. When Controlled Porosity Osmotic Pump is placed in aqueous environment the water soluble component of coating dissolves and forms micropores in membrane and water diffuses inside the core through micro porous membrane, setting up an osmotic gradient and thereby controlling the release of drug. The rate of release from controlled porosity osmotic pump is dependent on

- Level of soluble component in coating
- Coating thickness
- Osmotic pressure across the membrane
- Solubility of drug in tablet core.

Multi-particulate delayed release system

Pellets containing drug with or without osmotic agent are coated with semi permeable membrane which on contact with aqueous environment results in penetration of water in core and forms a saturated solution of soluble component. The osmotic pressure difference results in rapid expansion of membrane, which leads to the formation of pores. For controlled release drug is located at first orifice and for fast release drug layer located adjacent to second orifice. Push layer is located in between controlled and fast release layer (Figure No.18).

The dispenser comprises a housing that has first- and second-wall sections in a slide able telescoping arrangement. The housing maintains integrity in its environment of use. The device consists of two chambers; the first contains the drug and an exit port, and the second contains an osmotic engine. A layer of wax-like material separates the two sections.

New Macromolecular osmotic pump Delivery

The advances in biotechnology have introduced many proteins and other macromolecules that have potential therapeutic applications. These macromolecules bring new challenges to formulation scientists, since the digestive system is highly effective in metabolizing these molecules, making oral delivery almost impossible, while parenteral routes are painful and difficult to administer. A potential carrier for oral delivery of macromolecules is polymerized liposomes[14]. Liposomes are lipid vesicles that target the drug to selected tissues by either passive or active mechanisms[15]. Advantages of liposomes include increased efficacy and therapeutic index, reduction in toxicity of the encapsulated agent, and increased stability via encapsulation. One major weakness of liposomes is the potential leakage of encapsulated drugs due to the stability of liposome. Unlike traditional liposomes, the polymerized liposomes are more rigid because of cross-linking and allow the polymerized liposomes to withstand harsh stomach acids and phospholipase. This carrier is currently being tested for oral delivery of vaccines.

Pulmonary route is also being utilized as route for delivery of macromolecules. The lung's large absorptive surface area of around 100 m^2 makes this route a promising alternative route for protein administration. Drug particle size is a key parameter to pulmonary drug delivery. To reduce the particle size, a special drying process called **glass stabilization technology** was developed. By using this technology, dried powder particles can be designed at an optimum size of 1 to 5 for deep lung delivery (Figure No.19)

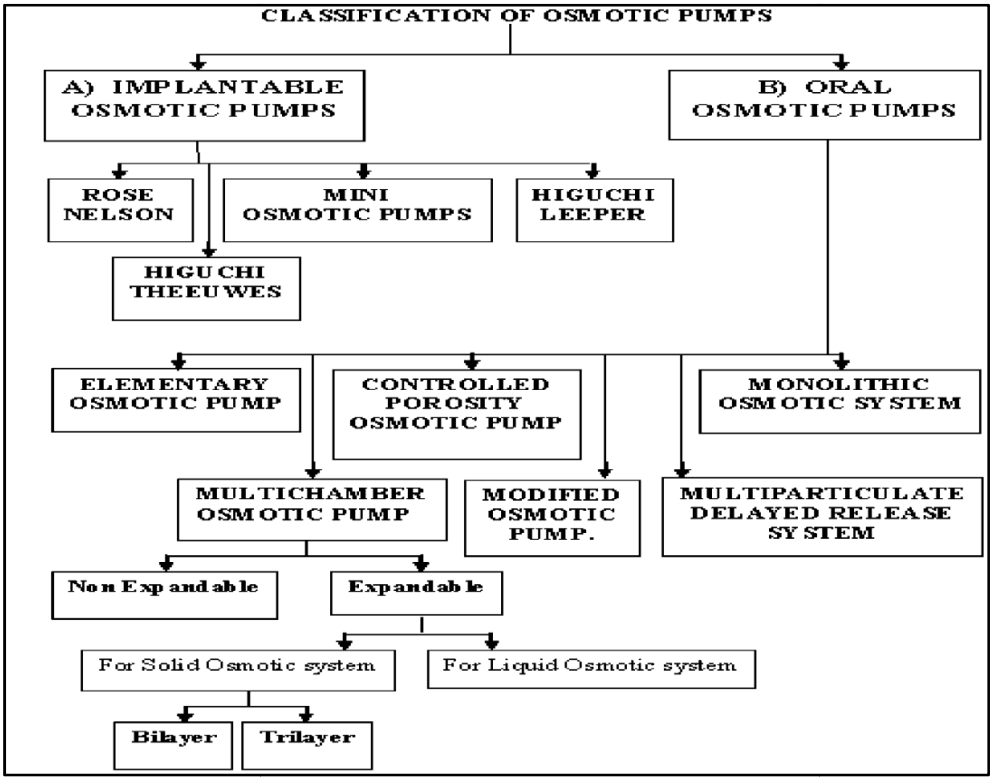

Figure No.1: Classification of Osmotic Pumps

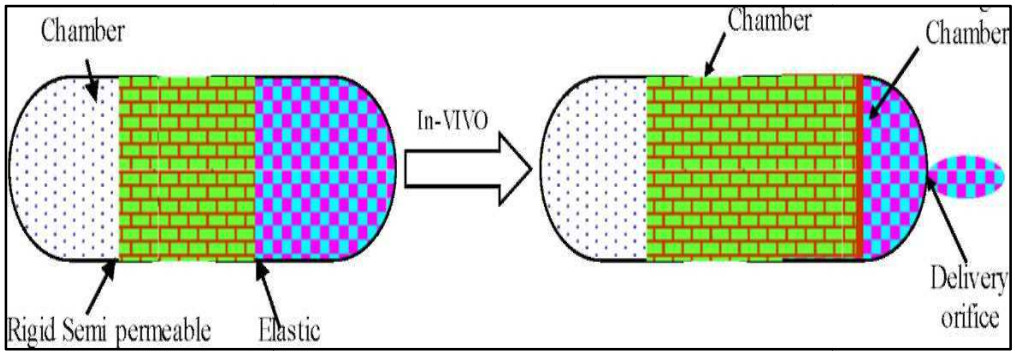

Figure No.2: Implantable Osmotic Pumps

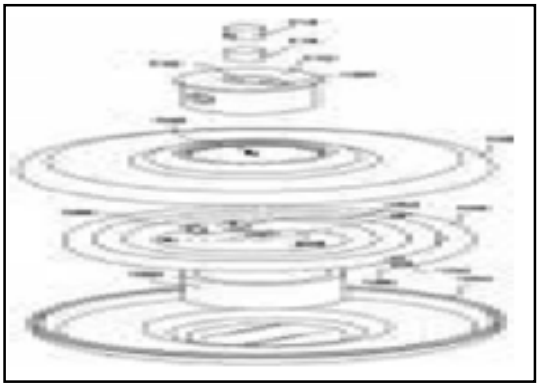

Figure No.3: Mechanism of Implantable Osmotic Pump

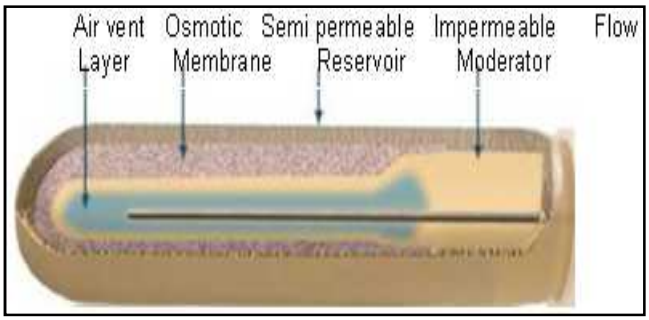

Figure No.4: Alzet osmotic pump

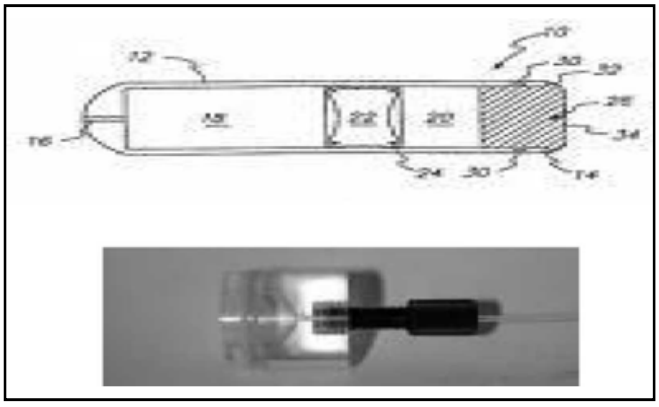

Figure No.5: Higuchi osmotic pump

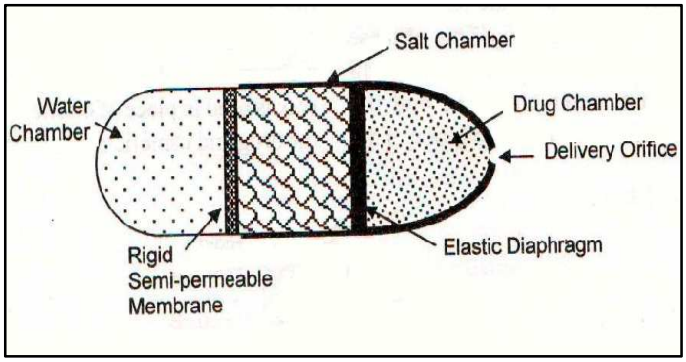

Figure No.6: Higuchi Leeper pump

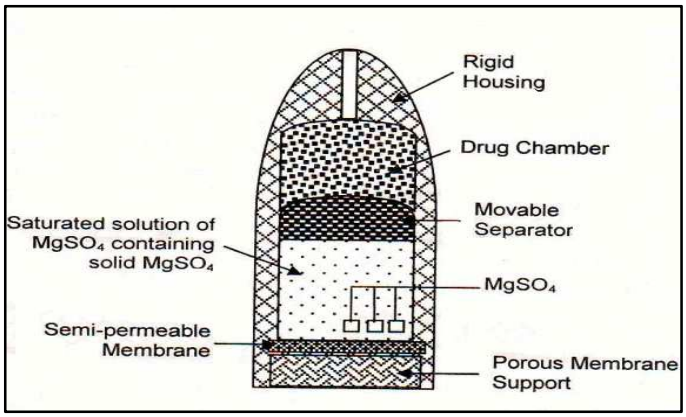

Figure No.7: Higuchi Theeuwes pump

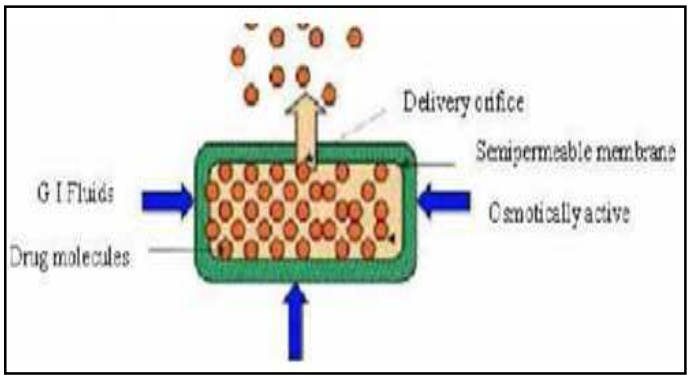

Figure No.8: Elementary Osmotic Pumps (EOP)
Core- API ± osmogents Coat- Semi permeable membrane with delivery orifice

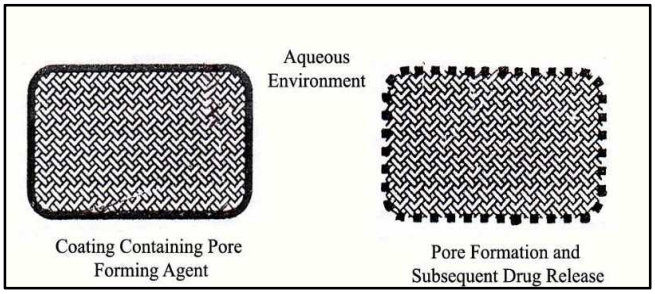

Figure No.9: Push pull osmotic pump

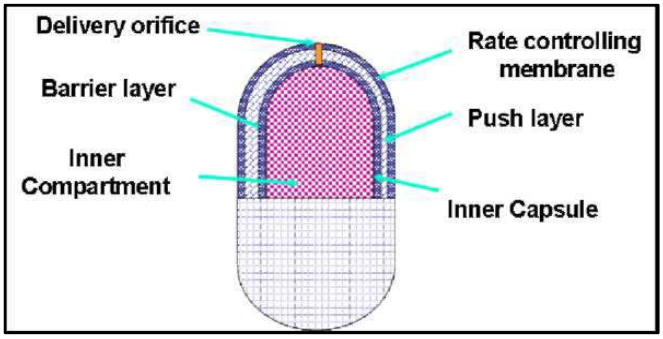

Figure No.10: Liquid oral osmotic systems

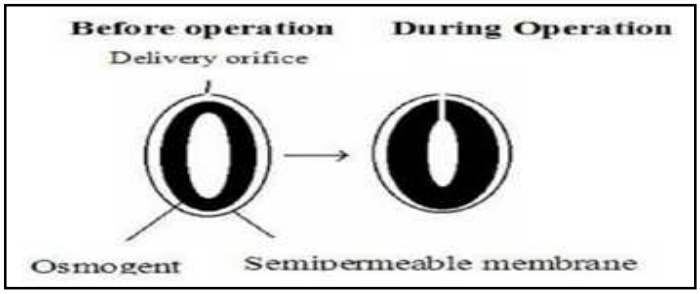

Figure No.11: Delayed liquid bolus delivery system

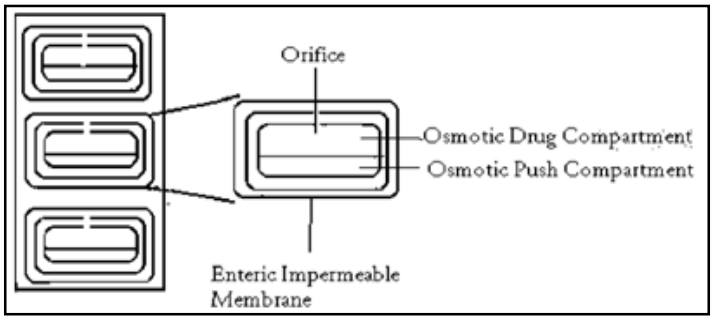

Figure No.12: Illustration of OROS-CT

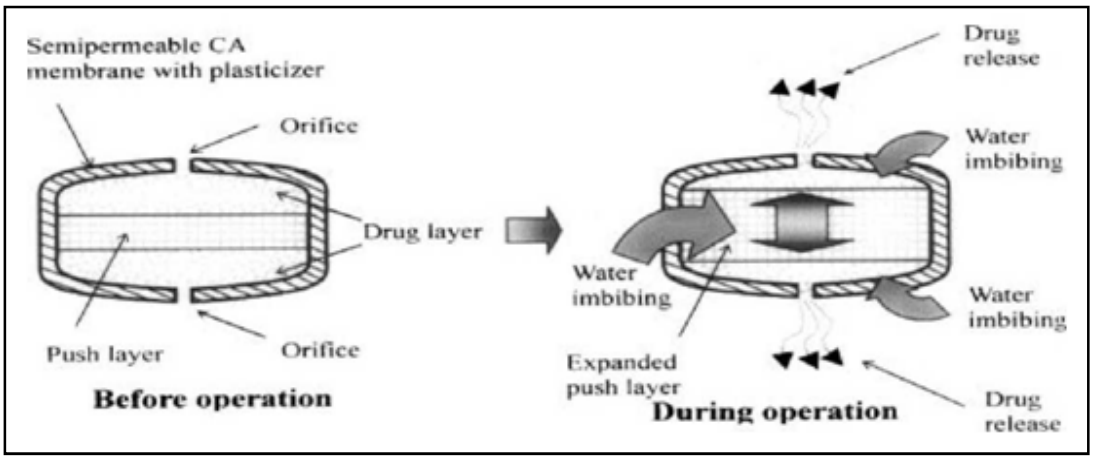

Figure No.13: Sandwiched osmotic pump

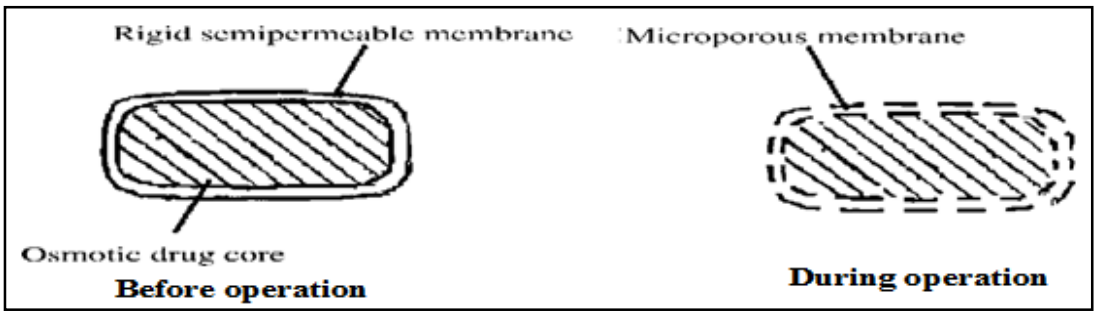

Figure No.14: Schematic diagram of controlled porosity osmotic pump before and during operation Osmotic bursting osmotic pump

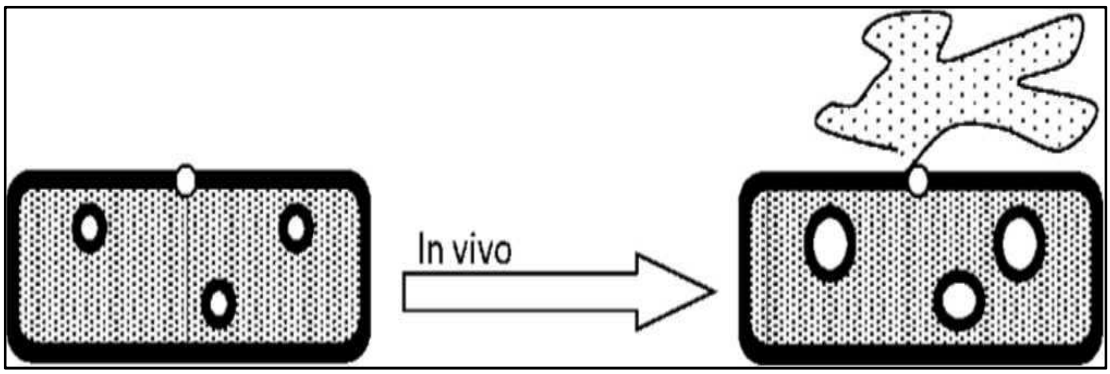

Figure No.15: Osmotic pump for insoluble drugs

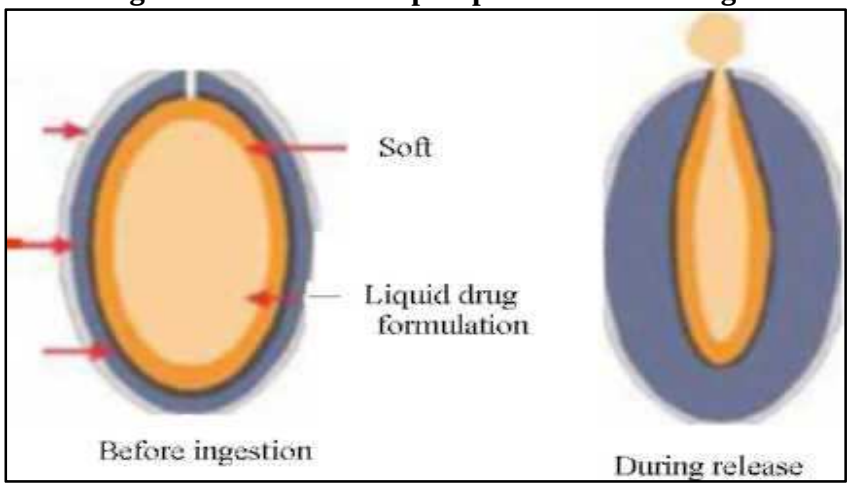

Figure No.16: Liquid osmotic system

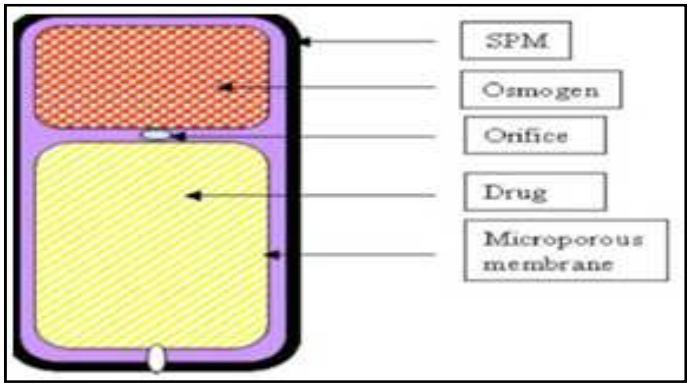

Figure No.17: Non Expandable Eop Tablet

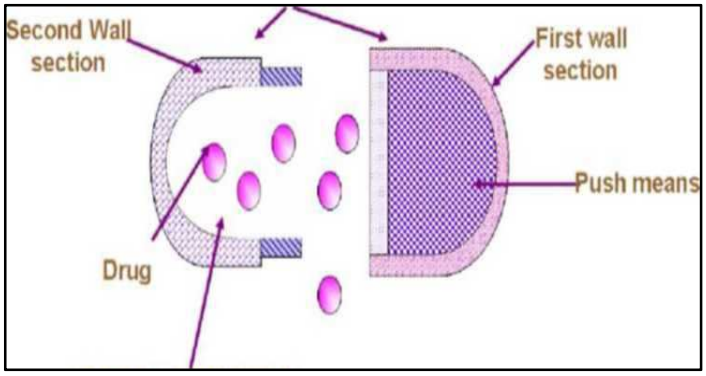

Figure No.18: Multi-particulate Delayed Release System

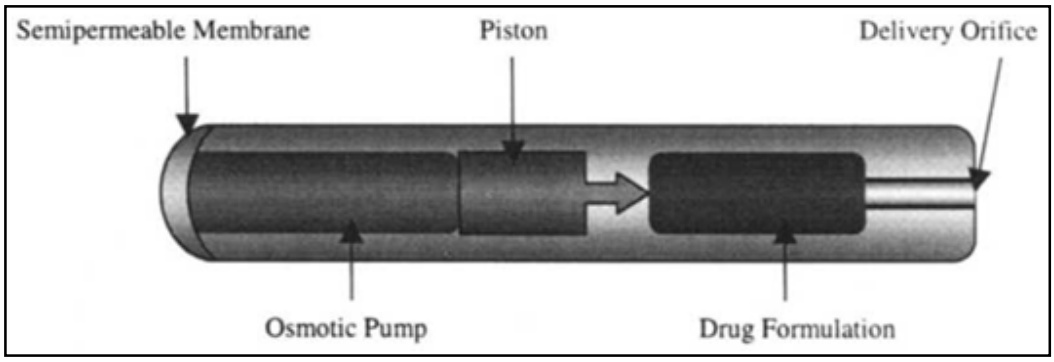

Figure No.19: Implantable Osmotic Pump

CONCLUSION

In Osmotic Drug Delivery system (ODDS), osmotic pressure provides the driving force for drug release. Major advantage is controlled drug release by zero order. The ODDS mainly reside in their capacity to deliver a drug at predetermined rate, independent of physiological parameter such as food intake, patient age, and pH of G. I. tract. Most of the ODDS device is designed by modifying the Rose-Nelson pump and Higuchi-Theeuwes pump. There are many marketed product long term therapy for diabetes, hypertension, other chronic disease of ODDS. Other than Oral ODDS implant that work on osmotic principle are promising for wide variety of molecule for long period of time. In the biotechnology industry there are many newer and potent drug are discovered they need to deliver such a constant in constant rate, the ODDS play important role in future. Now a day's large variety of ODDS technology available allows an interesting adaptation of the system to the drug property and the dosage strength.

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