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OSMOTIC PUMP DRUG DELIVERY- A NOVEL APPROACH

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Osmotic pump, controlled-porosity osmotic pump tablet, Osmosis, osmotic pressure, Zero-order release, Oral osmotic systems

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ABSTRACT

Conventional drug delivery systems are known to provide an immediate release of drug, in which one cannot control the release of the drug and cannot maintain effective concentration at the target site for longer time. Controlled drug delivery systems offer spatial control over the drug release. Osmotic pumps are most promising systems for controlled drug delivery. The present review is concerned with the study of drug release systems which are tablets coated with walls of controlled porosity. When these systems are exposed to water, low levels of water soluble additive is leached from polymeric material i.e. semi permeable membrane and drug releases in a controlled manner over an extended period of time. Drug delivery from this system is not influenced by the different physiological factors within the gut lumen and the release characteristics can be predicted easily from the known properties of the drug and the dosage form. Osmotic devices which are tablets coated with walls of controlled porosity are the most promising strategy based systems for controlled drug delivery.

INTRODUCTION

Conventional drug delivery systems have slight control over their drug release and almost no control over the effective concentration at the target site. This kind of dosing pattern may result in constantly changing, unpredictable plasma concentrations. [1] Drugs can be delivered in a controlled pattern over a long period of time by the controlled or modified release drug delivery systems. They include dosage forms for oral and transdermal administration as well as injectable and implantable systems. For most of drugs, oral route remains as the most acceptable route of administration. Certain molecules may have low oral bioavailability because of solubility or permeability limitations. Development of an extended release dosage form also requires reasonable absorption throughout the gastro-intestinal tract (GIT). [21] Oral drug delivery has been popular and the most widely utilized route of administration than other routes that have been explored for the systemic delivery of drugs. Conventional oral drug delivery systems are known to provide an immediate release of drug, in which one cannot control the release of the drug and effective concentration at the target site. [5] In this drug delivery system in order to achieve as well as to maintain the drug concentration within the therapeutically effective range, it is often necessary to take this type of drug delivery system several times a day. [32] This results in a significant fluctuation in drug levels. [16] So in recent year a focus has been on the development of novel drug delivery systems1**.** In this system, the drug dose and dosing interval are optimized to maintain drug concentration within the therapeutic window, thus ensuring efficacy while minimizing toxic effects.

Osmosis

Osmosis refers to the process of movement of solvent molecules from lower concentration to higher concentration across a semi permeable membrane

Principles of Osmosis

The first report of an osmotic effect dates to Abbenollet {1748}. But Pfeffer obtained the first quantitative measurement in 1877. In Pfeffer experiment a membrane permeable to water but impermeable to sugar is used to separate a sugar solution from pure water. A flow of water then takes place into the sugar solution that cannot be halted until a pressure π is applied to the sugar solution. Pfeffer showed that this pressure, the osmotic pressure π of the sugar solution is directly proportional to the solution concentration and the absolute temperature. Within few years, Vant

Hoff had shown the analogy between these results and ideal gas laws by the expression $\pi = Ø\ c\ RT$ Where, p = Osmotic pressure, π = osmotic coefficient, c = molar concentration, R = gas constant T = Absolute temperature. Osmotic pressure is a colligative property, which depends on concentration of solute that contributes to osmotic pressure. Solutions of different concentrations having the same solute and solvent system exhibit an osmotic pressure proportional to their concentrations. Thus a constant osmotic pressure, and thereby a constant influx of water can be achieved by an osmotic delivery system that results in a constant zero order release rate of drug.

Osmotic pressure for concentrated solution of soluble solutes commonly used in controlled release formulation are extremely high ranging from 30 atm for sodium phosphate up to 500 atm for a lactose-fructose mixture, as their osmotic pressure can produce high water flow across semi permeable membrane. The osmotic water flow through a membrane is given by the equation $dv\backslash dt = A\ Q\ \Delta\ \pi\backslash\ L$ Where $dv\backslash dt$ = water flow across the membrane of area A in cm2, L = thickness, Q = permeability and $\Delta\ \pi$ = the osmotic pressure difference between the two solutions on either side of the membrane. This equation is strictly for completely perm selective membrane that is membrane permeable to water but completely impermeable to osmotic agent.

HISTORY OF OSMOTIC DRUG DELIVERY SYSTEM:

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. [25] In1970- Alza Corporation made several simplifications in Rose-Nelson pump. The Higuchi- Leeper pump is modified version of Rose-Nelson pump. [23] 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. [35] This pump consists of a rigid housing, and the semi permeable membrane is supported on a perforated frame. It has a salt chamber containing a fluid solution with excess salt. [19] 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 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 semi permeable 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. [29] 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. [14] 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. [20]

Classification of Osmotic Pump

The OCODDS can be conveniently classified in to following types

Single Chamber Osmotic Pump Elementary Osmotic Pump (EOP)

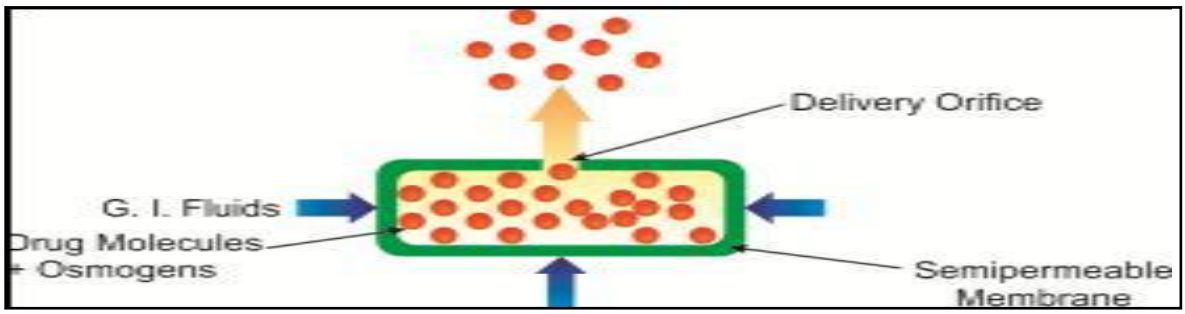
Rose-Nelson pump was further simplified in the form of elementary osmotic pump, which made osmotic delivery as a major method of achieving controlled drug release. Elementary osmotic pump shown in Figure 1 was invented by Theeuwes in 1974 EOP is the most basic device made up of a compressed tablet. [11] The EOP consists of an osmotic core with the drug, surrounded by a 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. [16] The rate of imbibitions of water is determined by the fluid permeability of the membrane and the osmotic pressure of the

compressed tablet. [18] 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. Normally EOP deliver 60 – 80 % of its content at constant rate but it has short lag time of 30 – 60 minute. It is applicable formoderately soluble

Figure 1: Elementary osmotic pump



Limitation

1. SPM should be 200-300µm thick to withstand pressure
2. □ Thick coatings lowers the water permeation rate
3. □ Applicable mostly for water soluble drugs

Multi Chamber Osmotic Pump Push Pull Osmotic Pump (PPOP)

The two-layer push–pull osmotic tablet system appeared in 1980s. Push pull osmotic pump is a modified elementary osmotic pump through, which it is possible to deliver both poorly water soluble and highly water soluble drugs at a constant rate. The push–pull osmotic tablet

Consists of two layers, one containing the drug and the other an osmotic agent and expandable Agent. [24] A semi-permeable membrane that regulates water influx into both layers surrounds the system. 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. [30] The osmotic attraction in the drug layer pulls water into the compartment to form in situ a suspension of drug. [4] The osmotic agent in the nondrug layer simultaneously attracts water into that compartment, causing it to expand volumetrically, and the expansion of nondrug layer pushes the drug suspension out of the delivery orifice. [7]

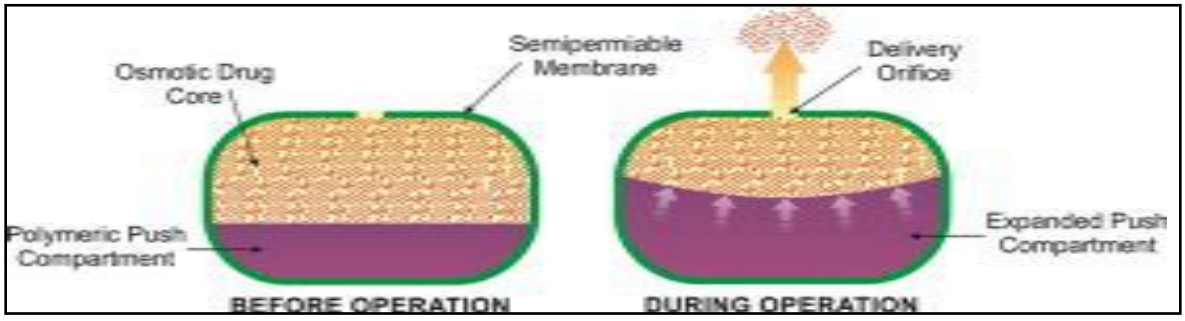


Figure 2: Push pull osmotic pump

Limitation

- Complicated laser drilling technology should be employed to drill the orifice next to the drug compartment.

Specific Types:-

Controlled Porosity Osmotic Pump

The pump can be made with single or multi-compartment 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. [12] 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. [37] 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. [34] All of these variable are under the control of the designer and do not vary under physiological condition, leading to the robust performance. The rate of flow of water into the device can be represented as

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

Where

dv/dt = Rate of flow of water

k = Membrane permeability

A = Area of the membrane

Dp = Osmotic pressure difference

DR = Hydrostatic pressure difference

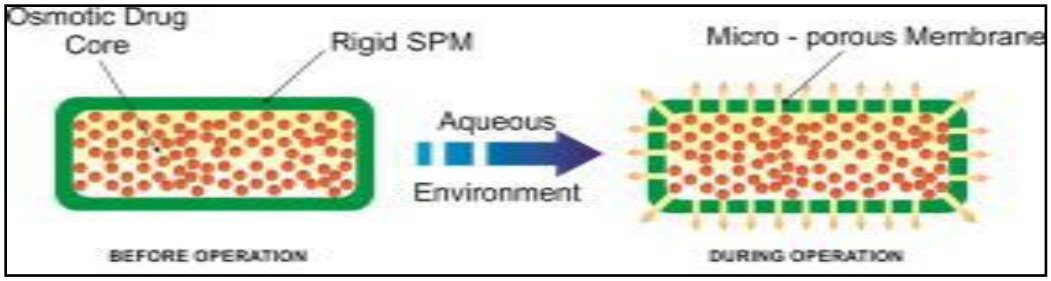


Figure 3: Controlled porosity osmotic pump

Limitation

- ✓ Drug release from the osmotic system is affected to some extent by the presence of food.
- ✓ Retrieval of therapy is not possible in the case of unexpected adverse events.

OROS – CT 53

OROS-CT (Alza corporation) is used as a once or twice a day formulation for targeted delivery of drugs to the colon. The OROS-CT can be a single osmotic agent or it can be comprised of as many as five to six push pull osmotic 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. [18] At the same time flowable gel is formed in the drug compartment, which is pushed out of the orifice at a rate, which is precisely controlled, by the rate of water transport across the semi-permeable membrane. Incorporation of the cyclodextrin-drug complex has also been used as an approach for delivery of poorly water soluble drugs from the osmotic systems. Ex. Sulfobutylether-β-cyclodextrin sodium salt serves as a solubilizer and osmotic agent. [10]

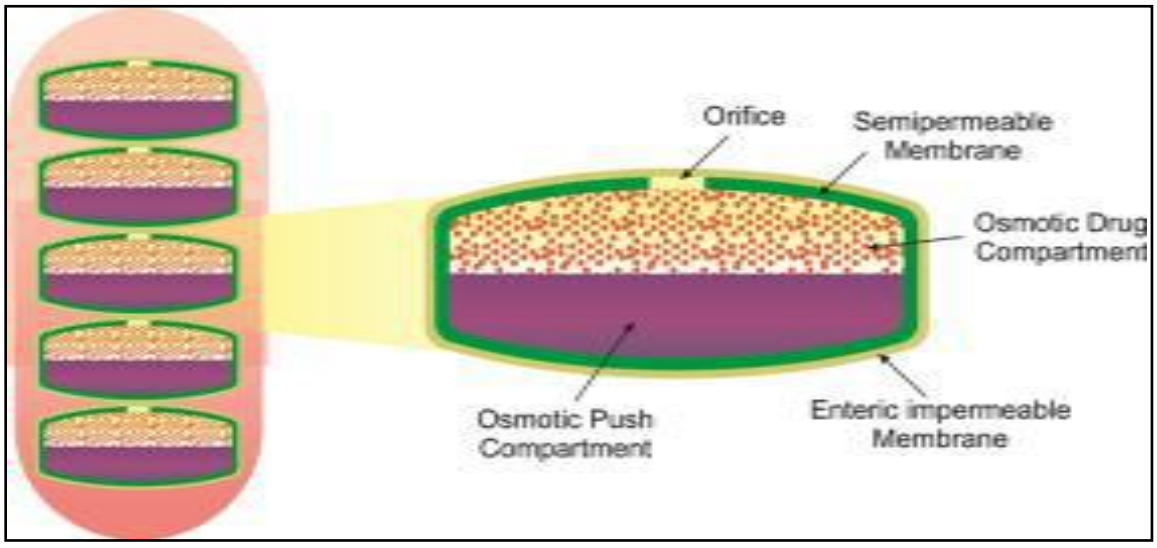


Figure 4: OROS – CT

Liquid Oral Osmotic System (L-OROS)

Various LOROS systems available to provide controlled delivery of liquid drug formulations Include L-OROS hard cap, L-OROS soft cap, and a 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. [27] 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 at the delivery Orifice. Whereas L-OROS hard cap and L-OROS soft cap systems are designed to provide continuous drug delivery, the L-OROS delayed liquid bolus delivery system is designed to Deliver a pulse of liquid drug. [3] The delayed liquid bolus delivery system comprises three Layers: a placebo delay layer, a liquid drug layer, and an osmotic engine, all surrounded by a rate controlling semi-permeable membrane (SPM). The delivery orifice is drilled on the placebo layer end of the capsule shaped device. When the osmotic engine expands, the placebo is released first, delaying release of the drug layer. [26] Drug release can be delayed from 1 to 10 hours, depending on permeability of the rate controlling Membrane and the size of placebo. [2]

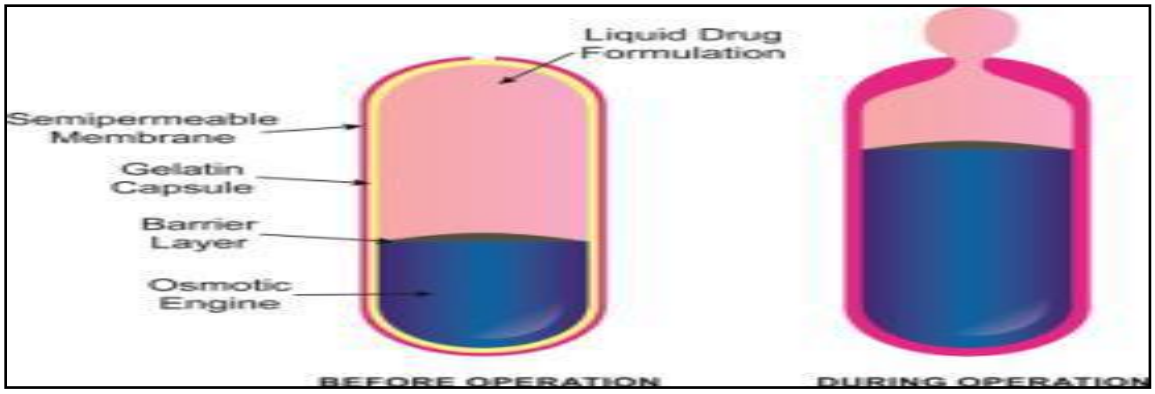


Figure 4: Liquid Oral Osmotic System

Sandwiched Osmotic Tablet (SOT) 49

In this a tablet core 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 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.

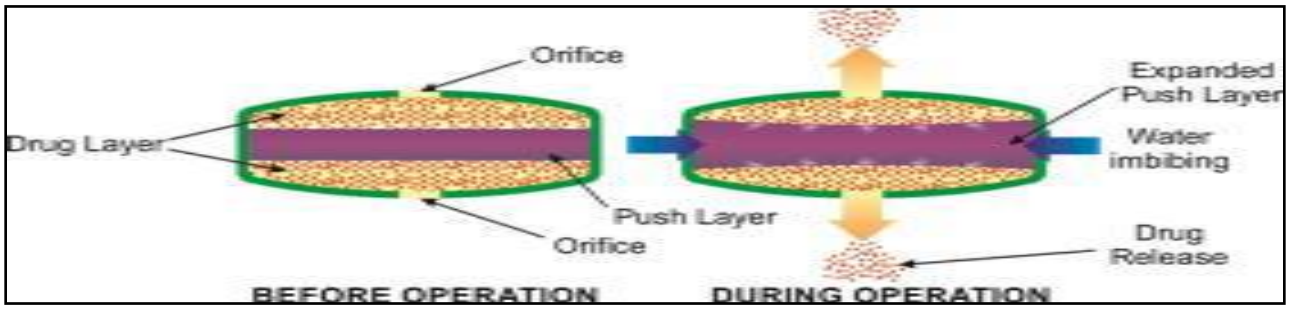


Figure 6: Sandwiched osmotic tablet

Telescopic Capsule for Delayed Release58, 59

This device consists of two chambers, the first contains the drug and an exit port, and the Second contains an osmotic engine. [9] 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. [8] 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. [13] 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. [28] 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. [22]

Osmotic Bursting Osmotic Pump52

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. [43] 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. [41]

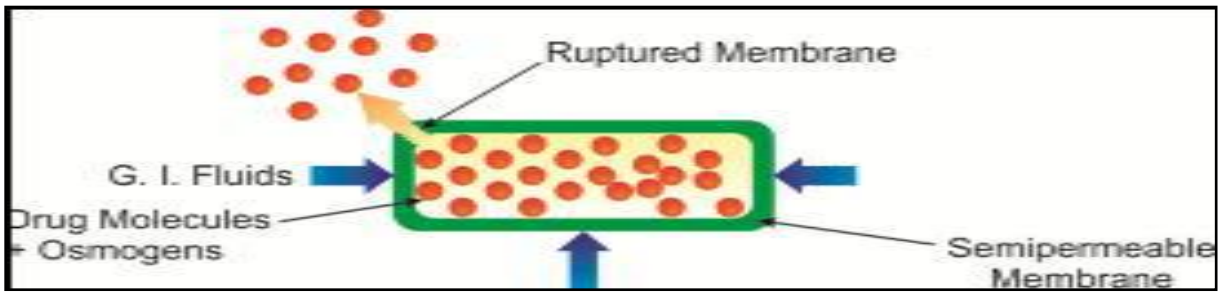


Table 1: Marketed products of osmotic pump.

Product name	Active pharmaceutical ingredient	Design of osmotic pump
Acutrim	Phenylpropanolamine	Elementary pump osmotic pump [9]
Alpress	LP Prazosin	Push-pull osmotic pump [2]
Cardura	XL Doxazosin	Push-pull osmotic pump [34]
ChronogesicTM	Sufentanil	Implantable osmotic system [8]
Covera HS	Verapamil	Push-pull osmotic pump with time delay [48]
Ditropan XL	Oxybutinin chloride	Push-pull osmotic pump [9]
Dynacirc CR	Isradipine	Push-pull osmotic pump [34]
Efidac 24	Pseudoephiderine	Elementary pump osmotic pump [8]
Efidac 24	Chlorpheniramine meleate	Elementary pump osmotic pump
Glucotrol XL	Glipizide	Push-pull osmotic pump [11]
Invega	Paliperidone	Push-pull osmotic pump [8]

COMPONENTS OF OSMOTIC DRUG DELIVERY SYSTEMS8,9

Osmotic pumps essentially contain a drug and semi Permeable membrane. The semi permeable membrane usually contains a plasticizer and in some cases surfactants and also pore forming agents. A part form the above materials, common tableting aids such as lubricants, binders, diluents, glidants ,wetting agents etc. [39]

DRUGS

- Short biological half-life {2-6h}
- Highly potent drug
- Required for prolonged treatment

SEMIPERMEABLE MEMBRANE

Cellulose acetate is a commonly employed semi permeable polymer for the preparation of osmotic pumps. It is available in different acetyl content of 32% and 38% Polymers are agar acetate, amylase triacetate, betaglucan, acetate, poly (Vinyl methyl) ether copolymers, poly (orthoessters) poly acetals and selectively permeable poly (glycolic acid) and poly (lactic acid) derivatives can be used as semi-permeable film forming materials.

WICKING AGENTS

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, 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 in weight poly (vinyl pyrolidone) PVP, m-pyrol, bentonite, magnesium aluminum silicate, polyester and poly ethylene. SLS, colloidal silica and PVP are non swellable wicking agents. [48]

SOLUBILISING AGENTS

These are classified under three groups. Agents that inhibit crystal formation of the drugs or otherwise act by complexation with the drugs. E.g. PVP, poly (ethylene glycol) (PEG 8000) and alpha, beta gammacyclodextrins. A high HLB micelle- forming surfactant, particularly anionic surfactants (eg tween 20, 60 and 80, poly oxy ethylene or citrate.

Osmotic Agent

Osmotic components usually are ionic compounds consisting of either inorganic salts or hydrophilic polymers. Some of the osmotic agents that can be used for such systems are classified below. [45] Different type of osmogents can be used for such systems are categorized as water-soluble salts of inorganic acids like magnesium chloride or sulfate; lithium, sodium, or potassium chloride; sodium or potassium hydrogen phosphate; water-soluble salts of organic acids like sodium and potassium acetate, magnesium succinate, sodium benzoate, sodium citrate, sodium ascorbate; Carbohydrates like mannose, sucrose, maltose lactose; water-soluble amino acids and organic polymeric osmogents, etc.

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 viscoelastic behavior 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; and diacetate- for low permeability. Tri ethyl citrate Diethyl tartarate or Diacetin- for more permeable films. [40]

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. The typical solvents include methylene chloride, acetone, methanol, ethanol, isopropyl alcohol, butyl alcohol, ethyl acetate, cyclo hexane, carbon tetrachloride, water etc.

FACTORS AFFECTING DRUG RELEASE RATE

Solubility

For the osmotic system, solubility of drug is one of the most important parameters affecting drug release kinetics from osmotic pumps. [51] The kinetics of osmotic drug release is directly related to the drug solubility within the drug core. Assuming a tablet core of pure drug, the fraction of core released with zero-order kinetics is given by equation [28]. $F(z) = 1 – S/\rho$ (1) Where, F(z) is the fraction released by zero-order kinetics, S is the drug's solubility (g/cm3), and ρ is the density (g/cm3) of the core tablet. Drugs with a density of unity and the solubility of ≤ 0.05 g/cm3 would be released with ≥ 95% zero-order kinetics, according to Eq. (1). At the same time, highly water-soluble drugs would demonstrate a high release rate that would be zero-order for a small percentage of the initial drug load. Thus, the intrinsic water solubility of many drugs might prohibit them from incorporation into an osmotic pump.

Candidate drugs for osmotic delivery have water solubility in the range 50–300 mg/ml. Some of the approaches that have been used to modulate drug solubility within the core include. Co-compression of the drug with excipients, which modulate the drug's solubility within the core. [33] Use of effervescent mixtures to speed up the release of poorly soluble drug from the orifice [38].use of various cyclodextrin derivatives to solubilize poorly water soluble drug. Use of alternative salt form that has optimum water solubility [41]; (5) use of encapsulated excipients [42]; (6) use of lyotropic crystals [43,44]; (7) use of wicking agents.[45,46].

APIs for **osmotic** delivery should have water solubility in the desired range to get optimize

Drug release. However, by modulating the solubility of these drugs within the core, effective release patterns may be obtained for the drugs, which might otherwise appear to be poor candidate for **osmotic** delivery. Solubility-modifying approaches: Use of swellable polymers. vinyl acetate copolymer, polyethylene oxide have uniform swelling rate which causes drug release at constant rate.Use of wicking agents: These agents may enhance the surface area of drug with the incoming aqueous fluids. e.g. colloidal silicon dioxide, sodium lauryl sulfate, etc. **Ensotrol®** technology uses the same principle to deliver drugs via **osmotic** mechanism.

Use of effervescent mixtures. Mixture of citric acid and sodium bicarbonate which creates pressures in the **osmotic** system and ultimately controls the release rate. Use of cyclodextrin derivatives. They are known to increase solubility of poorly soluble drugs. The same phenomenon can also be used for the **osmotic** systems. Use of alternative salt form: Change in

salt form of may change solubility. Use of encapsulated excipients.Solubility modifier excipients used in form of mini-tablet coated with rate controlling membrane.Resin Modulation approach.Ion-exchange resin methods are commonly used to modify the solubility of APIs. Some of the resins used in **osmotic** systems are Poly (4-vinyl pyridine), Pentaerythritol, citric and adipic acids. Use of crystal habit modifiers: Different Crystal form of the drug may have different solubility, so the excipients which may change crystal habit of the drug can be used to modulate solubility. Co-compression of drug with excipients. Different excipients can be used to modulate the solubility of APIs with different Mechanisms like saturation solubility, pH dependent solubility. Examples of such excipients are organic acids, buffering agent, etc.

Compound or mixture	Osmotic pressure
Lactose-fructose	500
Dextrose-fructose	450
Sucrose-fructose	430
Mannitol-fructose	415
Sodium chloride	356
Fructose	335
Lactose-sucrose	250
Potassium chloride	245
Dextrose	82
Mannitol	38
Sodium phosphate tribasic.12h_2o	36
Potassium sulphate	39

Size of Delivery Orifice

To achieve an optimal zero order delivery profile, the cross sectional area of the orifice must be smaller than a maximum size to minimize drug delivery by diffusion through the orifice. Furthermore, the area must be sufficiently large, above a minimum size to minimize hydrostatic pressure build up in the system. [42] The typical orifice size in **osmotic** pumps ranges from 600µ to 1 mm. Methods to create a delivery orifice in the **osmotic** tablet coating are:

- Mechanical drill
- Laser drill: This technology is well established for producing sub-mille meter size hole in tablets. Normally, CO2 laser beam (without put wavelength of 10.6µ) is used for drilling purpose, which offers excellent reliability characteristics at low costs48, 49.
- Indentation that is not covered during the coating process50: Indentation is made in core tablets by using modified punches having needle on upper punch. This indentation is not covered during coating process which acts as a path for drug release in **osmotic** system.
- Use of leachable substances in the semi-permeable membrane.

EVALUATION[33,34,35]

Oral osmotic drug delivery systems can be evaluated for following**:**

Visual inspection: Visual inspection of the film for smoothness, uniformity of coating, edge coverage and luster.

Coating uniformity: The uniformity of coating among the tablets can be estimated by determining the weight, thickness and diameter of the tablet before and after the coating.

Coat weight and thickness: The coat weight and thickness can be determined from depleted devices following careful washing and drying of the film, using standard analytical balance and screw gauge, respectively.

Orifice diameter: The mean orifice diameter of osmotic pump tablet can be determined microscopically using pre calibrated ocular micrometer.

***In- vitro* evaluation**

The conventional USP paddle and basket type apparatus have been used for the *in vitro* release of drugs from oral osmotic system. USP described the use of commercial standard dissolution apparatus and commercial applied analytic standard dissolutions

Apparatus the dissolutions medium is generally distilled water as well as simulated gastric fluid (for 1st 2-4hr) and intestinal fluid have been used. The standard specifications, which are followed for oral controlled DDS, are equivalently applicable for oral osmotic

Pumps. [52]

***In- vivo* evaluation**

As the environment in the intestinal tract of the dog is quite similar to that of the human beings in terms of pH and motility, dogs have been widely used for in vivo delivery rate measurement of drug(s) from oral osmotic drug delivery systems and also to establish in vitro /in vivo correlation (IVIVC). [44] In vivo evaluation can also be performed in healthy human volunteers. Various pharmacokinetic parameters (Cmax, Tmax, AUC and MRT) and relative bioavailability are calculated.

Advantages of Osmotic Drug Delivery

Systems

Osmotic drug delivery systems for oral andparenterals use offer distinct and practical advantages over other means of delivery. The following advantages have contributed to the popularity of **osmotic** drug delivery systems55.

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

CONCLUSION

Development efforts of oral osmotic controlled drug delivery systems during recent years have been very dynamic with the emergence of new technologies and products. With the expiration of the oral osmotic controlled drug delivery systems primary patents and the increasing demand of health authorities for improved patient treatment compliance and tolerability, the oral osmotic controlled drug delivery systems S is primed to increase their market within oral modified-release dosage forms.

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