

# Oral osmotically-drug driven systems: an overview

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**Abstract:** Oral osmotically-driven systems has the capability to deliver medicine in an exceedingly sustained manner, freelance of the drug chemical properties, of the patient's physiological factors or However, access to those technologies has been restricted by the producing challenges. During this critique, we have a tendency to shall offer a summary of the last 30-years of OODS development, description the technologies, specific merchandise and their clinical use. General steering on technology choice is represented in light-weight of the recent advances within the field. Overall, oral osmotically-driven systems seem to be a promising technology for product lifecycle methods.

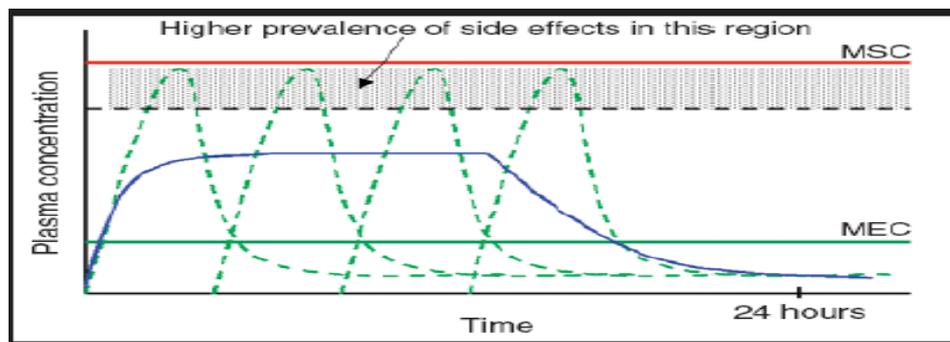
**Keywords:** diffusion pumps; osmotic drug delivery systems; oral diffusion systems; GITS; OROS; controlled drug delivery; review.

## INTRODUCTION:

The oral route for drug delivery is that the most well-liked, desirable technique for administrating therapeutically agents for general effects as a result of it's a Oral route is that the most ordinarily used route for drug administration. Though completely different route of administration area unit used for the delivery of medication, oral route stay the well-liked mode. Present controlled release drug delivery systems are for a maximum of 12 hours clinical effectiveness. Such systems are used for the drugs with short elimination half life

### Introduction to oral controlled drug delivery system:

The treatment of acute diseases or chronic sicknesses has been achieved by delivery of medication to the patients for several years. Nowadays these standard drug delivery systems area unit widely used. The term drug delivery are often outlined as techniques that are used to get the therapeutic agents inside the human body bod. These produce maximum stability, activity and bioavailability. For most drugs, conventional methods of drug administration are effective, but some of the drugs are unstable or toxic and they have narrow therapeutic index. However some drugs show unstable or nephrotoxic and have slender therapeutic ranges. Some medicine additionally possess solubility issues. In such cases, a way of continuous administration of therapeutic agent is fascinating to keep up mounted plasma levels as shown in Figure1.1



**Figure 1: Plasma drug concentration profiles for conventional tablet form or capsule formulation**

MEC = Minimum Effective Concentration; MSC = Maximum Safe Concentration.

To overcome these issues, controlled drug delivery systems were introduced 3 decades past. These delivery systems have variety of benefits over ancient systems (Table one.1) like improved potency, reduced toxicity, and improved patient convenience. The most goal of controlled drug delivery systems is to boost the effectiveness of drug therapies.

### Osmotically Controlled Drug Delivery Systems ( OCDDS)

OCDDS is one in all the foremost common and promising drug delivery system that's done by victimisation pressure level as a thrust for the management delivery of active. agent. The medicine that deliver through this technique aren't enthusiastic about hydraulics and pH scale conditions of the body. It's additionally potential to get higher release rates through these systems than through different diffusion-based systems. To meet patient's condition and demand numerous style/types of diffusion pumps for various medicinal drugs are available out there in market. Recently analysis in field of pharmaceutical shows development of many novel drug delivery

systems. The main motive of developed drug product is to be therapeutically effective with some further edges such as: Decreased side effects

- ✓ In chronic condition effectiveness could be greater
- ✓ Dose frequency could be decreased
- ✓ Delivery profile of the drug can be modified
- ✓ Simplified dosing schedule will improve patient medication use
- ✓ Consistent blood plasma level within the therapeutic window

### **Advantages of Osmotic Drug Delivery Systems**

Osmotic drug delivery systems for oral and parenterals use provide distinct and sensible advantages over other means of delivery. The following advantages have contributed to the recognition of diffusion drug delivery systems.

- 1) The delivery rate of zero-order is accomplishable with diffusion systems.
- 2) Delivery could also be delayed or periodic, if desired.
- 3) The release rate of osmotic systems is highly predictable and it can be programmed by modulating the releasing controlled parameters.
- 4) For oral systems, drug release is independent of gastric pH and hydrodynamic conditions.

### **DISADVANTAGES**

#### **1] Dose dumping:**

Dosing could be a development whereby comparatively profusion of drug in an exceedingly controlled formulation is speedily discharged, introducing probably nephrotoxic amount of the drug into circulation.

Dosing will result in fatalities just in case of potent medicine, that have a slender therapeutic index e.g. Barbiturate

#### **2] Less flexibility in accurate dose adjustment:**

In conventional dosage forms, dose adjustments are much simpler e.g. tablet can be divided into two fractions. In case of controlled release dosage forms, this appears to be much more complicated. Controlled release property may stray, if dosage form is fractured.

#### **3] Poor In-Vitro In-vivo correlation:**

In controlled release dosage form, the speed of drug release is deliberately reduced to realize drug release possibly over an outsized region of alimentary canal. Here it is so-called 'absorption window' which becomes important and may give rise to unsatisfactory drug absorption in-vivo despite excellent in-vitro release characteristics

#### **4] Increased potential for first pass clearance:**

Hepatic clearance is a saturable process. After oral dosing, the drug reaches the liver via hepatic portal vein. The concentration of drug reaching the liver dictates the quantity metabolized. Higher the drug concentration, greater is that the amount required for saturating an enzyme surface within the liver. Conversely, smaller the concentration found with the controlled release and a sustained release dosage form, lesser is that the possibility of saturating the enzyme surface. The possibility of reduced drug availability thanks to the primary pass metabolism is therefore greater with controlled release and sustained released formulation than with conventional dosage form.

#### **5] Patient variation:**

The period of time required for absorption of drug released from the dosage form may vary among individuals. Co-administration of other drugs, presence or absence of food and duration in alimentary canal is different among patients.

#### ***Other disadvantages of controlled released dosage forms are;***

- Administration of controlled release medication doesn't permit prompt termination of therapy. Immediate changes in drug levels during therapy, like could be encountered if significant adverse effects are noted, can't be accommodated.
- There is danger of an ineffective action or maybe absence of it if the therapeutic substance is poorly absorbed from GIT.
- Therapeutic agents that single dose exceeds 1 gm, the technical process requirements may make the product very difficult or sometimes impossible to organize.

- Therapeutic agents which absorbed by transport aren't good candidates for controlled release dosage form e. g. Riboflavin.
- Economic factors must even be taken under consideration , since more costly processes and equipments are involved in manufacturing of the many controlled release dosage forms.

While selecting a drug candidate for sustained release system we must take care . Drugs having following characteristics aren't suitable for sustained release systems:

1. Those which aren't effectively absorbed within the lower intestine
2. Those having short biological half-lives (12hrs) e.g. diazepam
3. Those with low therapeutic indices e.g. Phenobarbital
4. Those that no clear advantage of sustained release system e.g. griseofulvin.
5. Those with extensive first pass metabolism.
6. Those candidates with low solubility and/or active absorption

### Limitations of Osmotic Drug Delivery Systems

1. Special equipment is required for creating an orifice within the system.
2. Duration of the system within the body varies with the gastric motility and food intake.
3. It's getting to cause irritation or ulcer because of release of saturated solution of drug.

### Need for Developing Odds

1. To decreases dose related side effect.
2. To minimizes rate of administration.
3. To supply controlled release and
4. To extend patient compliance

### Principles of Osmosis

The first information of an osmotic effect dated to Abbenollet (1748). But Pfeffer obtained the primary quantitative measurement in 1877. In Pfeffer investigation, a membrane porous to water but opposing to sugar is employed to separate a sugar solution from pure water. A flow of water then takes place into the sugar solution that can't be halted until a pressure  $\pi$  is useful to the sugar solution. Pfeffer showed that this pressure, the pressure  $\pi$  of the sugar solution is straightly relative to the solution concentration and thus the temperature. Within few years, Van't Hoff had shown the resemblance between these results and perfect gas laws by the express:

$$\pi = \emptyset C R T$$

Where,

$\emptyset$  = pressure ,

$\pi$  = osmotic coefficient,

C= molar absorption,

R = universal gas constant,

T = temperature.

Osmotic pressure could also be a colligative property, which depends on concentration of solute that contributes to pressure. Solutions of dissimilar concentrations having the similar solute and solvent system disclose a pressure relative to their concentrations. Thus a mild pressure and there by a unbroken influx of water are often achieved by an osmotic delivery system that outcomes a unbroken zero order release rate of drug. pressure for concentrated solution of soluble solutes typically utilized in controlled release formulation are chiefly high ranging from 30 atm for sodium phosphate up to 500 atm for a lactose-fructose mixture, as their pressure can generate high water flow across semi permeable membrane.

The osmotic water flow through a membrane is given by the equation;

$$dv/dt = A Q \Delta \pi / L$$

Where,

$dv/dt$  = water stream across the membrane of area A in  $cm^2$ ,

$L$  = thickness,

$Q$  = permeability,

$\Delta \pi$  = the pressure dissimilarity between the 2 solutions on either side of the membrane.

This equation is strictly for totally perm discriminating membrane that's membrane porous to water but completely impermeable to osmotic agent.

#### **Basic parts of osmotically controlled drug delivery system (Osmotic Pumps):-**

1. drug
2. diffusion agent
3. semi semipermeable membrane
4. plasticizers
5. hydrophilic and hydrophobic chemical compound
6. wicking agent
7. wetting agent
8. coating solvent

#### **Types Of Diffusion Pumps**

Based on their style and so the state of active ingredient, diffusion delivery systems square measure typically classified as follows:

##### **1. Diffusion Delivery Systems For Solids**

###### **Type I: Single Compartment.**

In this style, the drug and so the diffusion agent square measure situated inside constant compartment and square measure enclosed by the membrane (SPM). Each the core parts square measure dissolved by water, that enters the core via diffusion. A limitation is that the dilution of drug answer with the diffusion answer that affects the discharge rate of the drug from the system. To boot, water-incompatible or waterinsoluble medication cannot be delivered effectively from a singlecompartment configuration.

###### **Type II: Multiple Compartments.**

In this style, drug is separated from the diffusion compartment by associate facultative versatile film that is displaced by the magnified pressure inside the encircling diffusion compartment, which, in turn, displaces the drug answer or suspension. Kind{the kind} II system inherently has larger utility than type I systems and should deliver medication at a desired rate freelance of their solubilities in water. One main advantage of these systems is their ability to deliver medication that square measure incompatible with usually used electrolytes or diffusion agents.

##### **2. Diffusion Delivery Systems For Liquids.**

Active ingredients in liquid type square measure tough to deliver from controlled unleash platforms as a result of they need a bent to leak in their native type. Therefore, liquid active agents usually square measure swallowed throughout a soft gelatin capsule that is enclosed by associate diffusion layer that, in turn, is coated with a membrane. Once the system takes up water from its surroundings, the diffusion layer squeezes the innermost drug reservoir. The increasing internal pressure displaces the liquid from the system by means of rupturing soft gelatin capsule.

#### **Osmotically controlled oral drug delivery:**

Oral osmotic drug delivery systems are principally classified as follows

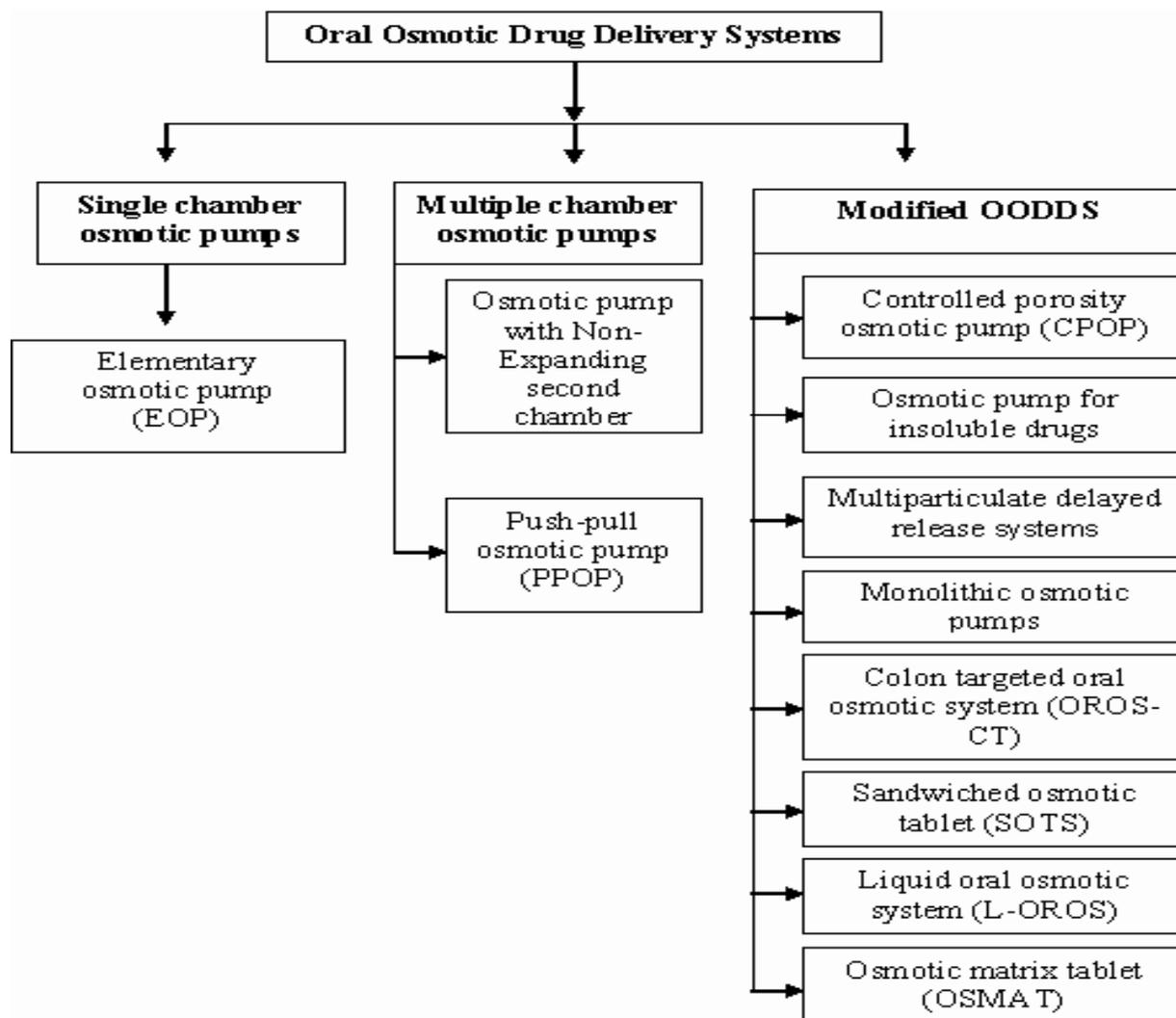


Figure.2. Schematic diagram of oral osmotic drug delivery system.

#### Elementary osmotic pump:

Elementary osmotic pump: Figure 3 shows schematic diagram of elementary osmotic pump (EOP), which in its simplest design, consists of an osmotic core (containing drug with or without an osmagent) coated with a semipermeable membrane (SPM). The dosage form, after coming with the aqueous fluids, imbibes with the water at a determined rate by the fluid permeability of the membrane and pressure of core formulation. This osmotic imbibition of water leads to formation of a saturated solution of drug within the core, which is dispensed at a controlled rate from the delivery orifice within the membrane. Although 60–80% of drug is released at an unbroken rate from Elementary osmotic pump, at a lag time of 30–60 min is observed in most of the cases because the system hydrates before zero-order delivery from the system begins. These systems are suitable for delivery of medicine having moderate water solubility.

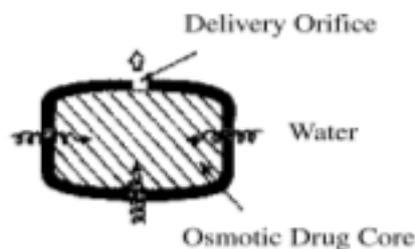


Figure 3: Elementary osmotic pump

#### Push-pull osmotic pump (PPOP):

It is a bilayer tablet coated with semipermeable membrane. The Push-pull osmotic pump system consists of two separate compartments usually by an elastic diaphragm present in it. The upper compartment contains the drug and is connected to the outside

environment via a small delivery orifice (Figure 1.3). A swellable polymer osmotic agent is present within the lower compartment, accounting for around 20-40 per cent of the tablet. The upper layer consists of drug and the delivery orifice.

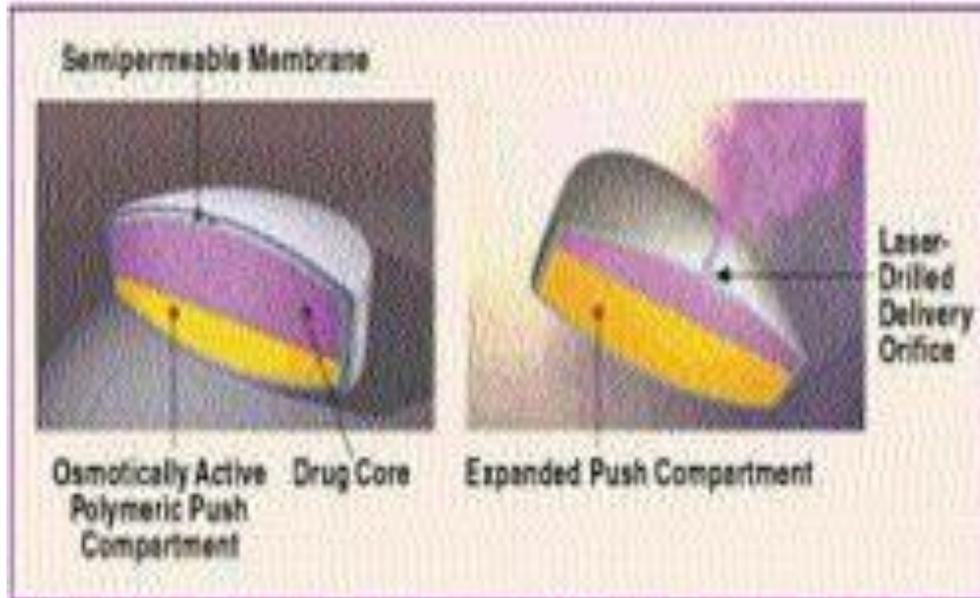


Figure 4: Push-pull osmotic pump

Pictorially, the mechanism of drug release from a PPOP is presented in scheme.

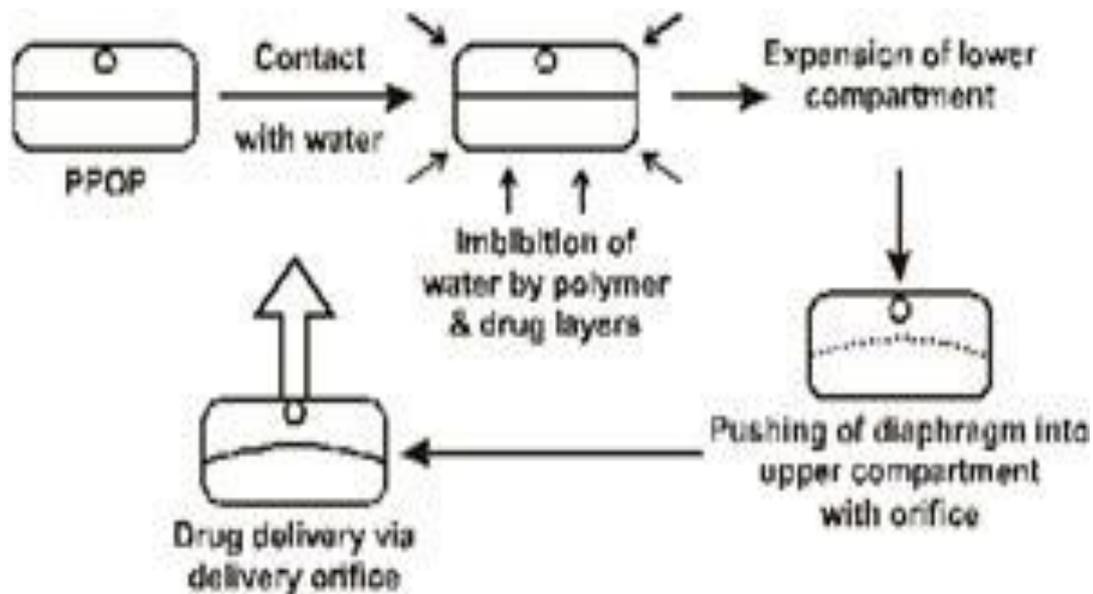
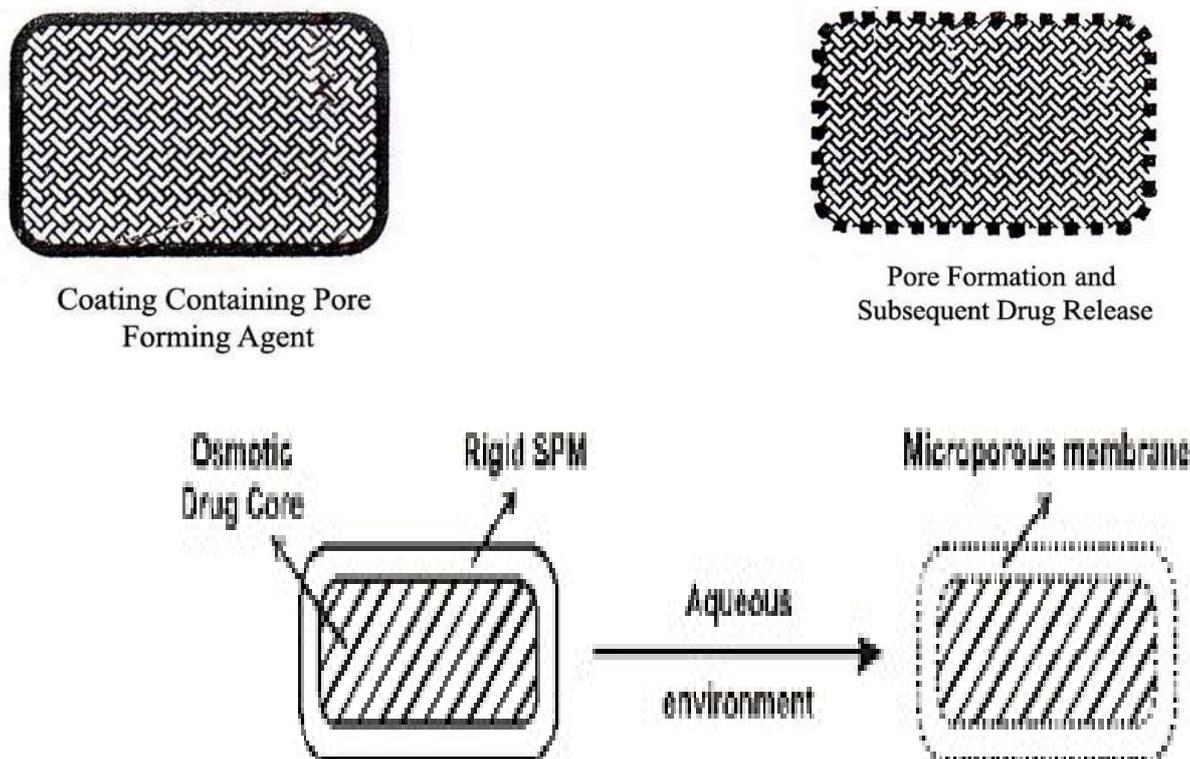


Figure 5: Mechanism of drug delivery

**Controlled porosity osmotic pump (CPOP):** It is an osmotic tablet wherein the delivery orifices (holes) are formed in situ through leaching of water soluble pore forming agents incorporated in SPM (e.g., urea, nicotinamide, sorbitol, etc). Drug release rate from CPOP depends on various factors like coating thickness, solubility of drug in tablet core, level of leachable pore forming agent(s) and therefore the pressure difference across the membrane.



**Figure 6: Mechanism of action of controlled porosity osmotic pump**

There are several obvious advantages to the Controlled porosity osmotic pump system. The stomach irritation problems are considerably reduced, as drug is released from the entire of the device surface rather from one hole. thus, no complicated laser-drilling is required because the holes are formed in-situ. This Scheme describes the drug releasing phenomenon from a typical Controlled porosity osmotic pump.

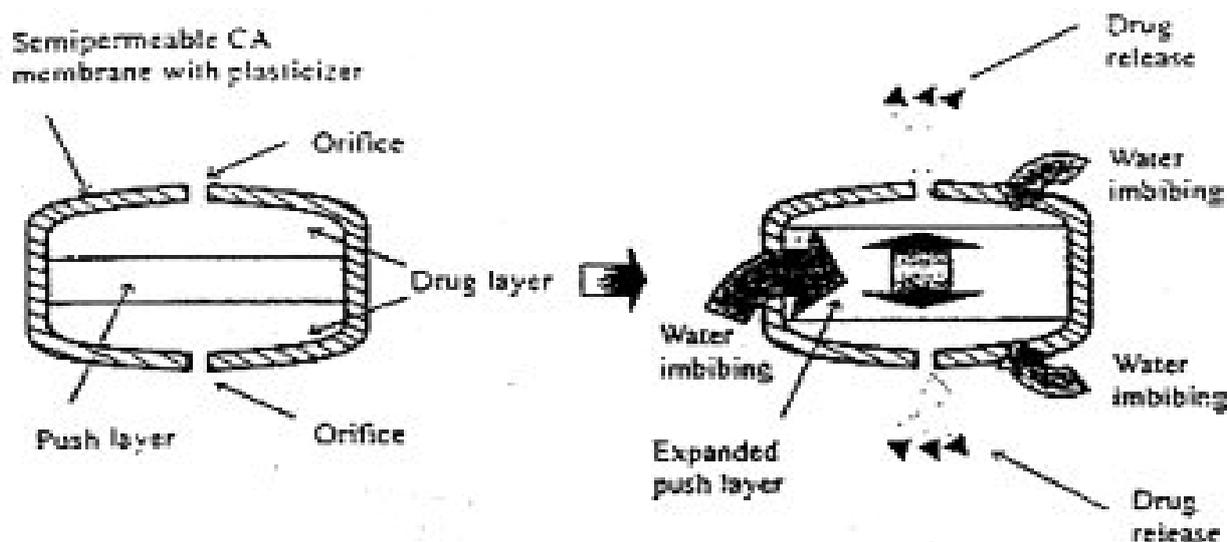
**Monolithic osmotic systems:** It constitutes a simple dispersion of a water-soluble agent in a polymeric matrix. When the system comes in contact with the aqueous environment, water imbibition by the active takes place rupturing the polymeric matrix capsule surrounding the drug, thus liberating it to the outside environment.

Initially, this process occurs at the outer environment of the polymer matrix, but gradually proceeds towards the inside of the matrix during a serial fashion. However, this system fails if more than 20 to 30 volume percent of the active agent is incorporated into the device, as above this level, significant contribution from the simple leaching of the substance takes place.

**Colon targeted oral osmotic system (OROS-CT):** It is a system with 5-6 enteric-coated push-pull osmotic units filled in hard gelatin capsule for targeted colonic drug delivery. After coming in touch with GI fluids, the gelatin capsule dissolves and therefore the enteric coating prevents the entry of fluids from stomach into the system.

As the OROS-CT 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, flowable gel is formed in the drug compartment, which is pushed out of the orifice at the rate precisely controlled by the rate of water transport across the SPM.

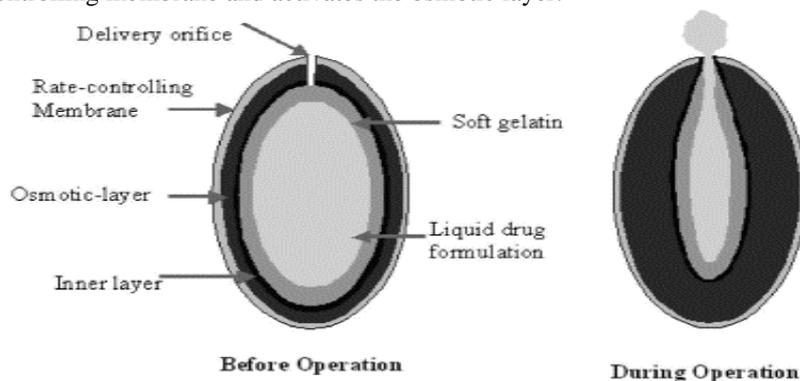
**Sandwiched osmotic tablets (SOTS):** it's composed of polymeric push layer sandwiched between two drug layers with two delivery orifices. When placed in the aqueous environment (Figure1.6), the middle push layer containing the swelling agents, swells and the drug is released from the delivery orifices. Drug is released from the 2 orifices situated on opposite sides of the tablet and thus SOTS are often suitable for drugs susceptible to cause local irritation of the gastric mucosa.



**Figure 7: Sandwiched osmotic tablet before and during the operation**

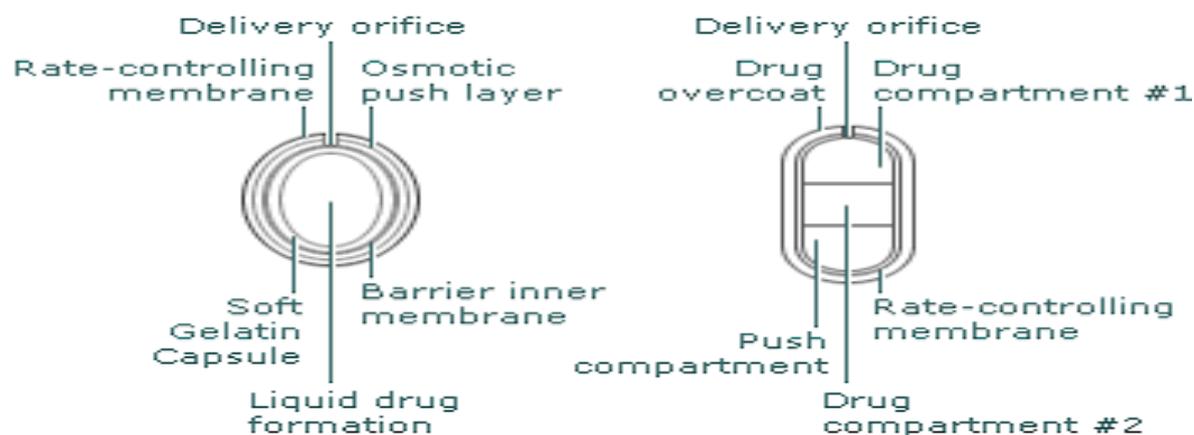
**Bursting osmotic pump:** In this system, delivery orifice is absent. As the GI fluid permeates into the pump, hydraulic pressure is built up inside the pump until the wall ruptures and the contents are released in the environment. It can be employed to control drug release by varying the thickness as well as the area of SPM.

**Liquid-oral osmotic (L-OROS) system:** Various L-OROS systems available to supply controlled delivery of liquid drug formulations include, L-OROS hardcap, L-OROS softcap and a delayed liquid bolus delivery system. Each of these systems includes a liquid drug layer, an osmotic engine or push layer and a SPM coating. When the system is in contact with the aqueous environment, water permeates across the rate-controlling membrane and activates the osmotic layer.



**Figure 8 Cross-sectional Diagram of Liquid Oral Osmotic System (L-OROS)**

The swelling of the osmotic layer takes place which leads to the event of hydrostatic pressure inside the system, thereby forcing the liquid formulation to be delivered at the delivery orifice. Whereas, L-OROS hardcap and L-OROS softcap 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. The delayed bolus delivery system comprises of three layers: a placebo delay layer, a liquid drug layer, and an osmotic engine, all surrounded by a rate controlling SPM. The delivery orifice is then drilled with using drilling on the placebo layer end of the capsule shaped device. When the osmotic engine expands, the placebo is released at first, and then results in delaying release of the drug layer. Drug release are often delayed from 1 to 10 hours, counting on permeability of the rate-controlling membrane and therefore the size of placebo.



**Figure 9: Liquid-oral osmotic (L-OROS) system**

## Conclusion

In the present review article, different types of osmotic drug delivery systems were studied and concluded that it is the most well-liked, desirable technique for administering therapeutically agents for general effects as a result of it's a Oral route is that the most ordinarily used route for drug administration.

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