



Received on 18 January, 2016; received in revised form, 22 February, 2016; accepted, 14 March, 2016; published 01 June, 2016

ORAL OSMOTIC DRUG DELIVERY SYSTEM: A REVIEW

Neetu Khatri *¹, Sarika Nikam ¹ and Ajay Bilandi ²

Padmashree Dr. D.Y. Patil College of Pharmacy, Akurdi, Pune ¹, Maharashtra, India

Seth G. L. Bihani S. D. College of Technical Education ², Sriganganagar, Rajasthan, India

Key words:

Osmotic pump, Controlled drug delivery, Dosing frequency and Therapeutic effect.

Correspondence to Author:

Neetu Khatri


Assistance Professor
(Department of Pharmaceutics)
Padmashree Dr. D.Y. Patil College of
Pharmacy, Akurdi, Pune

Email: neetukhatri111@yahoo.com

ABSTRACT: Osmosis is physical phenomenon that has been comprehensively studied by scientist in various disciplines of science and engineering. Osmotic devices are the most promising strategy based system for controlled delivery of drug. Conventional drug delivery has little 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 fluctuation in plasma concentration. Drug can be delivered in a controlled over a long period of time by the process of osmosis. Osmotic pump offers much compensation over other controlled release devices i.e. they improve patient compliance with reduced dosing frequency and are easy to formulate and prolong therapeutic effect with uniform blood concentration. They are most reliable controlled drug delivery system is not influenced by different physiological factor with in the gut lumen and the release characteristics can be predicted easily from the properties of the drug and the doses form. In this paper, various type of osmotically controlled pump with basic component and factor affecting has been discussed briefly.

INTRODUCTION: Oral drug delivery is the most preferred and convenient choice as the oral route provides maximum active surface area among all drug delivery system for administration of various drugs ¹. In conventional oral drug delivery systems, there is little or no control over release of the drug and effective concentration at the target site can be achieved by irregular administration of excessive doses.

This kind of dosing pattern result is fluctuation in therapeutic plasma concentrations, leading to marked side effects in some cases. Moreover, the rate and extent of absorption of drug from conventional dosage forms may vary greatly depending on factors such as presence of excipients, physicochemical properties of the drug, various physiological factors such as presence or absence of food, pH of gastro intestinal tract, gastro intestinal motility and so on. Uncontrolled rapid release of drug may cause local gastro intestinal or systemic toxicity. Hence, various approaches are made in designing the formulations, which will overcome the disadvantages of conventional dosage forms, which include sustained/controlled drug delivery system. There are three main classes

QUICK RESPONSE CODE	DOI: 10.13040/IJPSR.0975-8232.7(6).2302-12
	Article can be accessed online on: www.ijpsr.com
DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7(6).2302-12	

of controlled-release drug delivery system; transdermal, intravenous, and oral systems². Oral osmotically controlled release (CR) delivery systems exploit osmotic pressure for controlled delivery of active agents³. Drug release from these systems is independent of pH and other physiological parameters to a large extent and it is possible to modulate the release characteristics by optimizing the properties of drug and system². Alza Corporation R of USA was the first to develop an oral osmotic pump.

Principle and basic concept of osmotic drug delivery system:

It is based on the principle of osmotic pressure. Osmotic pressure is a colligative property, which is dependent on concentration of solute that contributes to osmotic pressure. Solutions of different concentrations having the same solvent and solute system show an osmotic pressure proportionate to their concentrations. Thus a constant osmotic pressure, and thereby a constant influx of water can be achieved by an osmotic drug delivery system. This results a constant zero order release rate of drug. The rate of drug release from osmotic pump depends on the osmotic pressure of the core and the drug solubility; hence, these systems are suitable for delivery of drugs with moderate water solubility.

Osmotic pressure is proportionate to temperature and concentration and the relationship can be described by following equation.

$$\pi = n_2 RT$$

Where, π = osmotic coefficient

n_2 = molar concentration of solute in the solution

R = gas constant

T = Absolute temperature³

Basic formulation concept:

Osmotic drug delivery devices are composed of an osmotically active drug core, which is surrounded by a rate controlling semipermeable membrane. Osmotic drug delivery system differ from diffusion based systems in that the way of delivery of the active agents is driven by an osmotic gradient somewhat than the concentration of drug in the device. In the most simple type of osmosis-

controlled drug release the following sequence of steps is involved in the release process:

- Osmotic transport of liquid in to release unit.
- Dissolution of drug within the release unit.
- Convecting transport of a saturated drug solution by pumping of the solution through a single orifice through pores in the semi permeable membrane⁴.

The delivery of active agent from oral osmotic systems is controlled by the influx of solvent through the semi-permeable membrane, which in turn transfers the active agent to the outside environment. Considering the relationship between osmotic pressure and chemical potential, the rate of water transport through the membrane can be

$$\frac{dv}{dt} = \frac{A}{h} L_p(\sigma\Delta\pi - \Delta p) \quad (1)$$

Where dv/dt is water influx, L_p is mechanical permeability, s is the reflection coefficient, A and h are the membrane area and membrane thickness, and $\Delta\pi$ and Δp are the hydrostatic pressure differences, between the inside and outside of the system.

Hydrostatic pressure inside most osmotic drug delivery systems is generally less than 1 atmospheric pressure, though some systems may attain pressure as high as several atmospheres. The hydrostatic pressure differential is negligible:

$$\Delta\pi \gg \Delta p$$

Equation (1) can then be written as follows:

$$\frac{dv}{dt} = (A/h) k \Delta\pi \quad (2)$$

Where $k = L_p\sigma$. Therefore, k can be written as the effective permeability of the membrane.

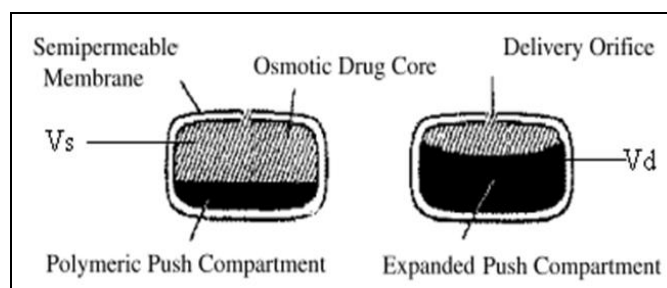


FIG. 1: OSMOTIC PUMP⁵

Fig.1 show that the osmotic pump demonstrate the semi permeable membrane and water influx in to the pump. Water permeates through the membrane and enters compartment V_s , causing it to expand: this extension compresses compartment V_d , and pushing drug out through the orifice. In equation (2), dV/dt represents the volume rate of change of the compartment indicated by V_s . if the compartment V_d is filled with a drug solution or suspension at concentration c and if the movable partition readily transmits displacement from compartment V_s to the compartment V_d , the rate of drug delivery (dm/dt) from the osmotic pump is given by following equation:

$$dm/dt = (dV/dt)c \quad (3)$$

Substituting in equation (2) for dV/dt ,

$$dm/dt = (A/h) k \Delta\pi c \quad (4)$$

Depending upon the design of the system, A , h , k , $\Delta\pi$, and c may vary with time:

$$dm/dt = [A(t)/h(t)] k(t)\Delta\pi(t)c(t) \quad (5)$$

Equation (5) can be written in term of the degree of hydration of the system (H):

$$dm/dt = (A_H/h) k \Delta\pi_H c \quad (6)$$

considering of equation (4) through (6) reveals that a variety of delivery rate profiles- increasing over time, zero order, or some combination of these are possible depending on the specific design of the osmotic system ⁶.

Factors that affect the drug release from osmotic delivery of drugs:

➤ The drug release from osmotic delivery device depends on many process and formulation variables, including curing treatment, plasticization, and properties of the core. Besides the water solubility of the drug, the solubility of the other core ingredients can also have a major influence on the drug release by generating an osmotic pressure gradient across the polymeric coating upon interaction with dissolution medium. The rate of drug release from osmotic pumps is dependent on the total solubility and the osmotic pressure of the core (drug). Various factor that

affect the release of drug from osmotic system are follows:

Orifice Size: Osmotic delivery systems contain at least one delivery orifice in the semipermeable membrane for drug release and the size of delivery orifice must be optimized in order to control the drug release from osmotic systems ⁵. To achieve an optimum zero-order delivery profile, the cross sectional area of the orifice must be smaller than a maximum size S_{max} to minimum drug delivery by diffusion through orifice. Moreover, the area must be sufficiently large, above a minimum size S_{min} , to minimize the hydrostatic pressure build in the device. Otherwise, the hydrostatic pressure can distort the membrane and affect the zero-order delivery rate of drug. Therefore, the cross sectional area of the orifice should be maintained between minimum and maximum values.

$$S_{min} = 5 \left[\left(\frac{L}{P_{max}} \right) \mu \left(\frac{dV}{dt} \right) \right]^{1/2}$$

Where,

dV/dt = volume of flux through an orifice

L = length of the orifice (usually the same as thickness of the membrane)

μ = viscosity of the drug solution flowing through the orifice

P_{max} = maximum tolerated hydrostatic pressure difference across the membrane before occurrence of deformation of the housing.

The maximum cross sectional area of the orifice is obtained by stipulating that the release rate must be smaller than a fraction f of the zero order pumping rates and is defined by following equation:

$$S_{max} = \frac{M_{tz} f L}{D_s C_s}$$

Where M_{tz} is the amount of the drug delivered in zero order manner, and D_s is the drug diffusion coefficient in the permeating solvent ². Instead, size of delivery orifice should not also be too large then; solute diffusion from the orifice may take place ⁵.

Methods to create a delivery orifice in the osmotic tablet coating are:

➤ Mechanical drill

➤ **Laser drill:** This technology is well established for producing sub-millimeter size hole in tablets. Normally, CO₂ laser beam (with output wavelength of 10.6μ) is used for drilling purpose, which compromises excellent reliability characteristics at low costs.

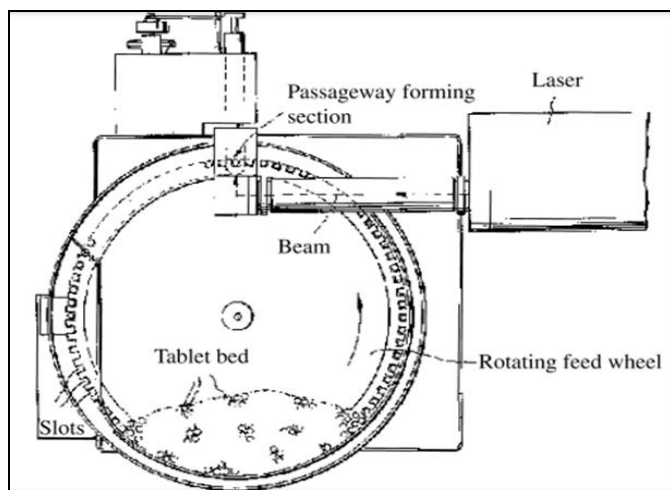


FIG. 2: TOP VIEW OF THE LASER HOLE-DRILLING SYSTEM FOR OSMOTIC DOSAGE FORMS⁵

➤ Indentation that is not covered during the coating process: This is made in core tablets by using improved punches having needle on upper punch and 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 coating: e.g. controlled porosity osmotic pump⁷.

Solubility:

The release rate of drug depends on the solubility of the solute inside the drug delivery device. Consequently, drugs should have sufficient solubility to be delivered by osmotic delivery^[3]. The kinetics of osmotic drug release is directly related to the solubility of the drug within the core. Assuming a tablet core of pure drug, the fraction of core released with zero-order kinetics is given by the following equation:

$$F(z) = 1 - S/\rho$$

Where $F(z)$ is the fraction of drug released by zero-order kinetics, S is the drug solubility (g/cm^3), and

ρ is the density (g/cm^3) of the core tablet. Drugs with a solubility of $\leq 0.05 \text{ g}/\text{cm}^3$ would be released with $\geq 95\%$ zero-order kinetics according to above equation. Though, the zero order release rate would be slow, due to the small osmotic pressure gradient. Conversely, highly water-soluble drugs would exhibit high release rate that would be zero-order for a small percentage of the initial drug load. Therefore, the intrinsic water solubility of many drugs might preclude them from incorporation into an osmotic pump². (Khavare1 NB et al. 2010) In the case of low solubility compounds, numerous alternative approaches may be employed and can be divided into two categories. First, swell-able polymers can be added that result in the delivery of poorly soluble drugs in the form of a suspension. Second, the drug solubility can be modified employing different methods³.

➤ Use of encapsulated excipients:

A capsule device coated with asymmetric membranes to deliver drugs having poor water-solubility (Fig. 2). In the examples, solubility of a poorly water-soluble drug such as glipizide was enhanced by incorporation of bicarbonate was used as encapsulated excipients (pH-controlling excipients) within the capsule device. The solubility modifier (meglumine), in the form of mini-tablets, was coated with a rate controlling membrane to prolong its availability within the core. Thus, the solubility of glipizide was improved leading to its prolonged release from the device⁵.

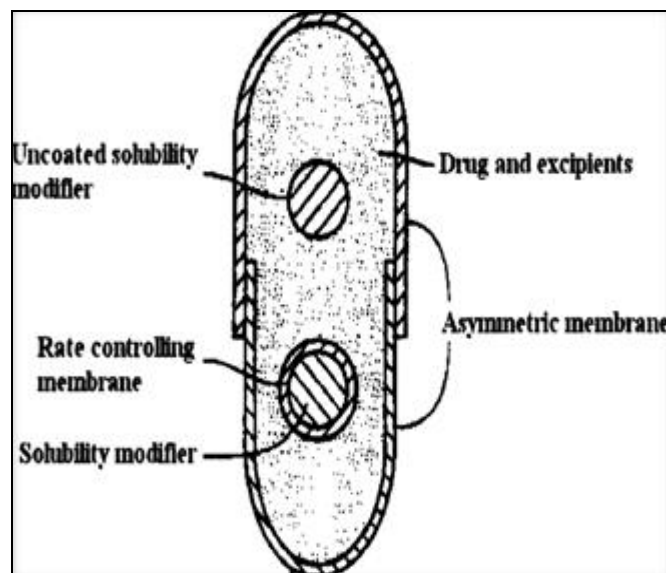


FIG.3: SCHEMATIC VIEW OF DELIVERY SYSTEM HAVING ENCAPSULATED EXCIPIENTS⁵

➤ **Use of cyclodextrin derivatives:**

These increase apparent drug solubility and dissolution through inclusion complexation or solid dispersion which is acting as hydrophilic carriers for drug with inadequate molecular characteristic for complexation, or as tablet dissolution enhancer for drug with high dose, with which use of a drug/cyclodextrin complex is difficult, eg, paracetamol. The same phenomenon can also be used for the osmotic systems⁷.

➤ **Use of swellable polymers:**

Polyethylene oxide, vinyl acetate copolymer have uniform swelling rate which causes drug release at constant rate⁸. Also, the pressure produced during swelling does not lead to rupture of the system⁵.

➤ **Use of wicking agents:**

These agents may increase the surface area of drug with the inward aqueous fluids. E.g. sodium lauryl sulfate and colloidal silicon dioxide, etc. Ensotrol® technology uses the same principle to deliver drugs via osmotic mechanism⁹.

➤ **Use of effervescent mixture:**

It can be another approach to deliver poorly water-soluble drugs from osmotic delivery systems. After administration, the effervescent mixture containing the drug is delivered under pressure through the delivery orifice in the membrane⁵. Effervescent mixture of citric acid and sodium bicarbonate generate carbon di-oxide which creates pressure in the osmotic system and finally the release drug at a constant rate⁷.

➤ **Co-compression of drug with excipients:**

Different excipients can be used to modify the solubility of drugs with different mechanisms like saturation solubility, pH dependent solubility. Examples of such excipients are organic acids, buffering agent, etc

➤ **Use of alternative salt form:**

Change in salt form of drug may change solubility. It is finding that the salt of drug is too soluble to maintain a saturated solution and hence zero order delivery for the anticipated delivery life of dosage form. Afterward osmotic pump is formulated with this salt form that give extended release up to 24 h.

➤ **Resin Modulation approach:**

Ion-exchange resin methods are commonly used to modify the solubility of drugs. Some of the resins used in osmotic systems are Poly (4-vinyl pyridine), Pentaerythritol, citric and adipic acids².

Osmotic Pressure:

The osmotic pressure π directly affects the release rate of drug. To achieve a zero-order release rate, it is crucial to keep π osmotic pressure constant by maintaining a saturated drug solution. Many times, the osmotic pressure generated by the saturated drug solution may not be sufficient to achieve the required osmotic pressure (driving force). In this case, other osmotic agents are added which enhance the osmotic pressure. For example, addition of bicarbonate salt not only delivers the necessary osmotic gradient but also prevents clogging of the orifice by precipitated drug by producing an effervescent action in acidic media⁸. (Gupta S. et al. 2011)

The osmotic pressure can also be found out by the Van't Hoff equation:-

$$\pi = CRT$$

Where:

π = Osmotic pressure of the solution, C = Molar concentration of the solute in the solution, R = Gas constant, T = Absolute temperature.

If required osmotic pressure is not obtained then a second compound is incorporated called as an osmotic attractant agent with the active agent into inclusion. The osmotic attractant is drawn from those compounds such as: having high osmotic pressure, do not degrade, don't interfere with the membrane or enclosed wall, do not interfere with action of the active drug molecule or the environment into which it is ultimately released, do not degrade very quickly¹⁰.

Semi permeable Membrane:

The choice of a rate-controlling membrane is an important characteristic in the formulation development of osmotic systems. The importance of rate-controlling membrane in the drug release can be easily recognized. Drug release from osmotic systems is independent of the pH and

agitational intensity of the gastrointestinal tract to a large extent. This is because of selectively water permeable membrane and effective isolation of dissolution process from the gut environment. The thickness of membrane is usually kept between 200 and 300 μm ⁵.

Classification of oral osmotic pump

As oral route is the most popular route of administration, most of the osmotic systems are developed as oral drug delivery. It is possible to deliver active agent at zero-order release rate, independent of gastric pH and hydrodynamic conditions with these osmotically controlled drug delivery systems.

Types of oral osmotic pumps:

1. Single chamber osmotic pump: Elementary osmotic pump
2. Multi chamber osmotic pump: Push pull osmotic pump, Osmotic pump with non-expanding second chamber
3. Specific types: Controlled porosity osmotic pump, Osmotic bursting osmotic pump, Liquid OROS, Delayed Delivery Osmotic device, Telescopic capsule, Oros CT (colon targeting), Sandwiched oral therapeutic system, Monolithic osmotic system and OSMAT.

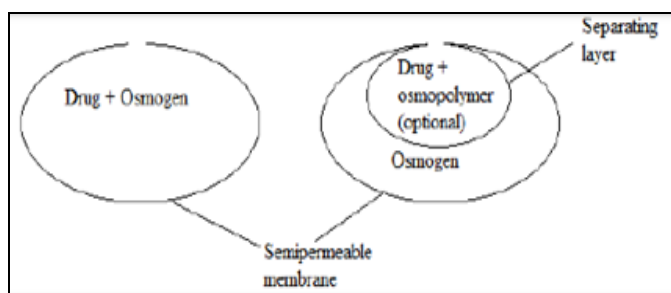


FIG. 4: SINGLE AND MULTICHAMBER OSMOTIC PUMP³

Single chamber osmotic pump: Elementary Osmotic Pump:

The elementary osmotic pump is a new delivery system. The basic Oros system, the elementary osmotic pump (EOP), was first described by Theeuwes in 1975¹¹. It delivers the active agent by an osmotic process at a controlled rate. Control resides in the water permeation characteristics of a semi permeable membrane surrounding the

formulating agent and the osmotic properties of the formulation⁸. The tablet consists of an osmotic core containing the drug which is surrounded by a semi permeable membrane laser drilled with delivery orifice. Following ingestion, water is immersed into the system dissolving the drug, and the resulting drug solution is delivered at the same rate as the water entering the tablet³ by osmosis. This displaces the drug in the core, which is then released from the orifice¹². The drawbacks of the elementary pump are that it is only suitable for the delivery of water soluble drugs³. They allow zero order delivery of drug.

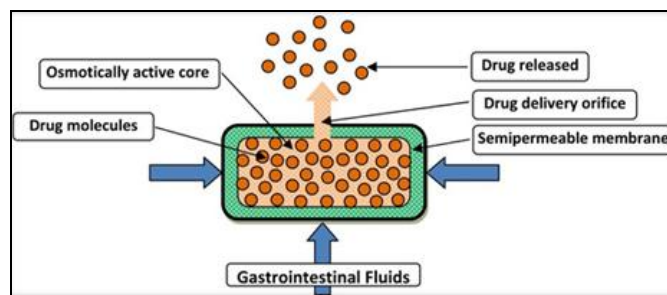


FIG.5: ELEMENTARY OSMOTIC PUMP¹³

Multi chamber osmotic pump:

Push pull osmotic pump: It is a bilayered tablet which is coated with a semipermeable membrane. Drug osmogen is present in the upper section & lower section consists of polymeric osmotic agent. A delivery orifice is drilled on the drug side of the tablet. When the system comes in contact with the gastric fluids, polymeric osmotic layer swells and pushes the drug layer thereby delivering the drug in the form of a fine dispersion through the orifice. They allow zero order delivery of drug¹⁴.

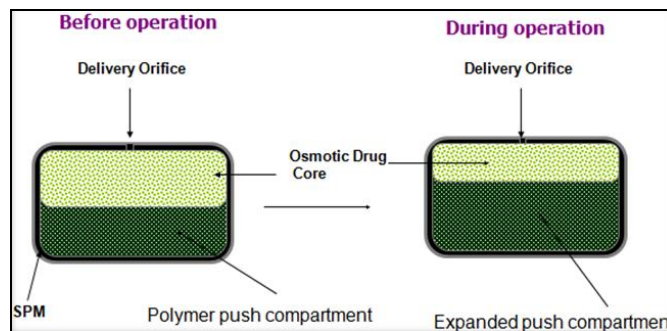


FIG.6: PUSH PULL OSMOTIC PUMP¹⁵

Osmotic pump with non- expanding second chamber: In this case there will be no expansion of second chamber and based on the functioning of this chamber, they are of two types. In the first

type, second chamber helps in dilution of drug solution. This is advantageous because some drugs cause the irritation when they are saturated. In second type, there are two chambers, one consists of the osmotic agent and the other consists of the drug. Primarily osmotic agent solution is formed which enters the drug solution and then their mixture is released out by means of semipermeable membrane present around the chamber¹⁶. Types of osmotic pumps. Available at <http://www.pharmainfo.net/satyajeethpandey/blog/types-osmotic-pumps>. Accessed on (12-03-2013)

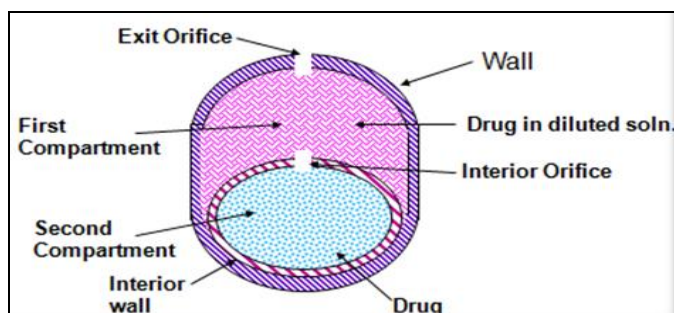


FIG. 7: OSMOTIC PUMP WITH NON- EXPANDING SECOND CHAMBER¹⁵

Specific types:

Controlled porosity osmotic pump:

It is an osmotic device wherein the delivery orifices are formed in situ through leaching of water soluble pore-forming agents incorporated in semipermeable membrane (E.g., urea, nicotinamide, sorbitol, etc.). Drug release rate from controlled porosity osmotic pump depends on various factors like coating thickness, level of leachable pore-forming agent(s) solubility of drug in tablet core, and the osmotic pressure difference across the membrane. There are several advantages characteristic to the system. The stomach irritation problems are significantly reduced, as drug is released from the whole of the device surface rather from a single hole. Further, no complicated laser-drilling unit is required because the delivery orifices are formed in situ.

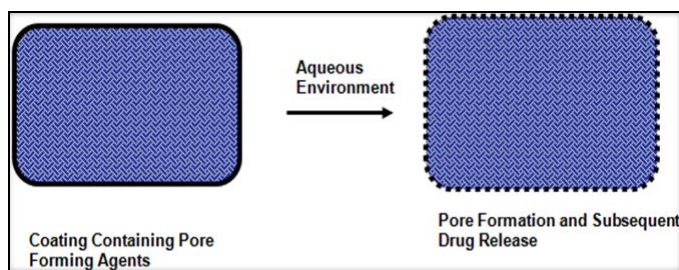


FIG 8: CONTROLLED POROSITY OSMOTIC PUMP¹⁵

Osmotic bursting osmotic pump:

This system is similar to an elementary osmotic pump except delivery orifice is absent and size may be smaller. When it is placed in an gastric fluids, water is imbibed and hydraulic pressure is built up inside until the semipermeable membrane ruptures and the content are released to the environment. Varying the thickness as well as the area the semipermeable membrane can control release of drug. This system is useful to provide pulsated release³.

Liquid Oral Osmotic system:

This allows the delivery of liquid drug formulations. A liquid formulation is particularly well suited for delivering insoluble drugs and macromolecules such as polysaccharides and polypeptides. Such molecules require external liquid components to assist in solubilization, dispersion, protection from enzymatic degradation, and promotion of gastrointestinal absorption¹¹. This device containing three-lamina first is rate controlling membrane, second is osmotic layer and third is soft gelatin capsule. During operation, water permeates across the rate controlling membrane and causes expansion of the osmotic layer resulting in to development of hydrostatic pressure inside the system which forces the liquid formulation out of the delivery orifice¹⁴.

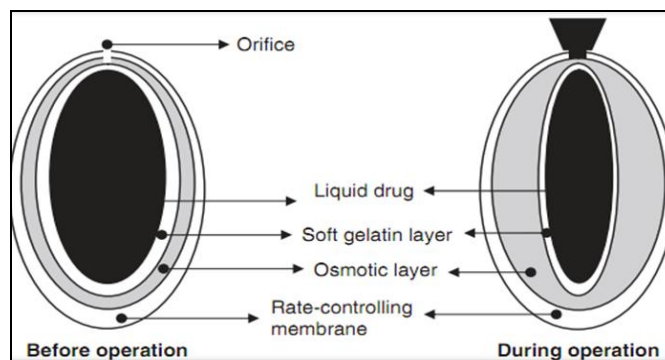


FIG.9: LIQUID ORAL OSMOTIC SYSTEM¹⁷

Delayed Delivery Osmotic device:

Because of semi permeable walls, an osmotic device integrally show lag time before drug delivery begins. Although this characteristic is usually cited as a drawback, it can be used advantageously. The delayed release of certain drug (drugs for early morning asthma or arthritis) may be beneficial.

Telescopic Capsule for Delayed Release:

This device consists of two chambers, the first chamber 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 mechanical 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. When fluid is imbibed in the device, the osmotic engine expands 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 flow of environmental fluid driven by the pressure enter the reservoir is minimal and consequently no agent is delivered for the period¹⁸.

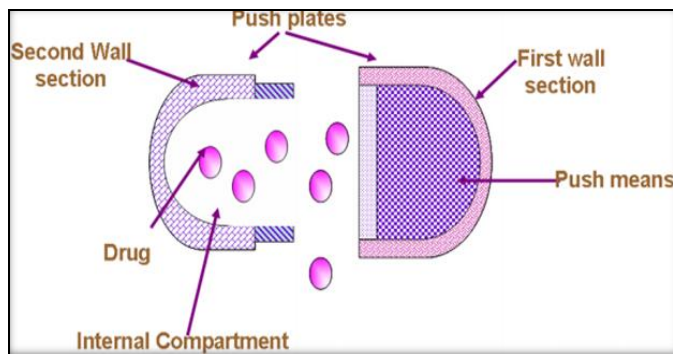


FIG. 10: TELESCOPIC CAPSULE FOR DELAYED RELEASE

Oros Colon Targeting:

It is used as a once or twice a day formulation for targeted delivery of drugs to the colon. This can be a single osmotic agent or it can be contained of as many as five to six push pull osmotic unit filled in a hard gelatin capsule. After coming in contact with the aqueous environment, gelatin capsule dissolved and the enteric coating prevents entry of fluids from stomach to the system when 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 membrane⁸.

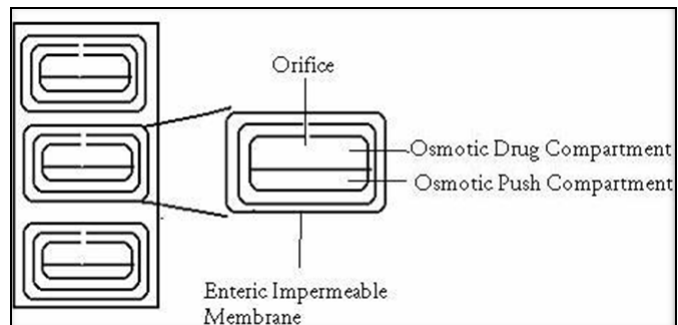


FIG.11: OROS CT (COLON TARGETING)³

Sandwiched oral therapeutic system:

In this system a tablet core composed of polymeric push layer sandwiched between two drug layers with two delivery orifices. When device is placed in the aqueous environment the middle push layer which containing the swelling agent swells and the drug is released from the two orifices situated on opposite sides of the tablet and thus these systems can be suitable for drugs prone to cause local irritation of the gastric mucosa¹⁹.

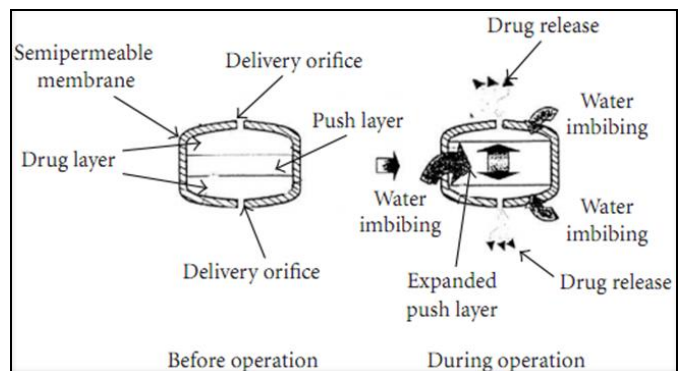


FIG.12: SANDWICHED ORAL THERAPEUTIC SYSTEM¹⁹

Monolithic osmotic system:

It constitutes a simple dispersion of water-soluble agent in a polymer matrix. When the system comes in contact in with the aqueous environment water imbibition by the active agents cause rupturing the polymer matrix capsule surrounding the drug this liberating it to the outside environment. Primarily 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 ⁸.

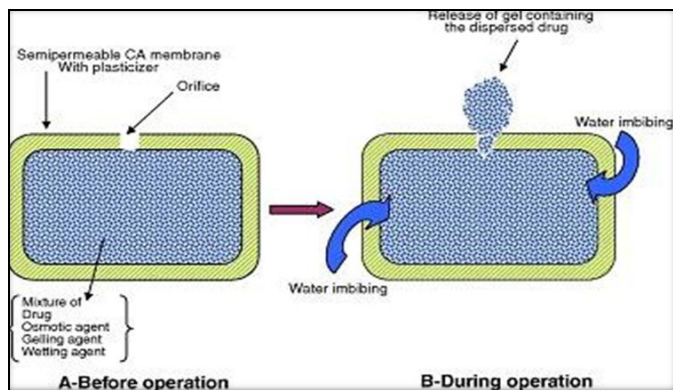


FIG.13: MONOLITHIC OSMOTIC SYSTEM ¹⁵

Osmotic Matrix Tablet (OSMAT):

This type of system utilizes the swells property of hydrophilic polymer, which swells and gels in aqueous medium forming a semipermeable membrane in situ. The release from this system is affected by the inclusion of osmogen with a matrix delivery of drug from OSMAT is independent of agitation & is low coast technology ¹⁴.

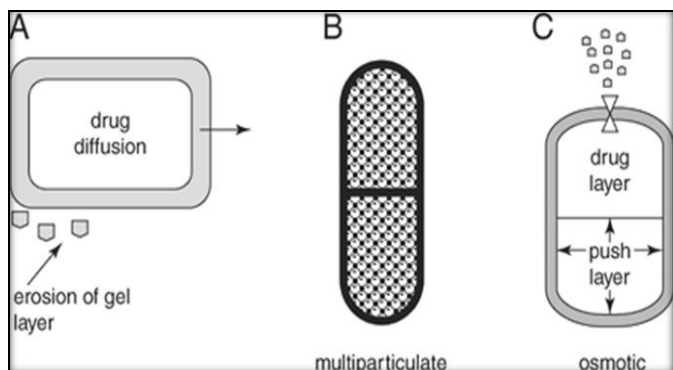


FIG. 14: OSMOTIC MATRIX TABLET (OSMAT)

Advantages of Osmotic Drug Delivery Systems:

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

- The zero-order drug release rate is achievable with osmotically controlled drug delivery system.
- Delayed or pulsed delivery may be possible.

- 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 ³.
- Drug release is independent of gastric pH and hydrodynamic condition.
- They are well characterized and understood.
- The release mechanisms are not dependent on drug.
- A high degree of in-vitro and in-vivo correlation (IVIVC) is obtained in osmotic systems ¹⁸.
- The rationale for this approach is that the presence of water in gastric region is relatively constant, at least in terms of the amount required for activation and controlling osmotically base technologies ⁸.

Disadvantages:

Osmotic Drug Delivery Systems have produced significant benefit in various therapeutic areas. Some systems have enhanced patient compliance, while other has minimized the side effect of their active compounds. However some limitations of osmotic drug delivery systems have been reported.

- Slightly higher cost than matrix tablet or multi particulates ion capsule dosage form.
- Gastro intestinal obstruction cases have been observed with the patient receiving Nifedipine tablet.
- Another case was reported for osmosin (Indomethacin OROS) is frequent occurrences of serious gastrointestinal reaction were observed leading to osmosin withdrawal.
- Magnetic resonance imaging (MRI) of tablet elucidates that non-uniform coating leadsto different pattern of drug release among the batches ¹⁰.

- If the coating process is not well controlled there is a risk of film defects, which results in dose dumping
- Size hole is critical
- Dose dumping
- Retrieval therapy is not possible in the case of unexpected adverse events ⁸.

Evaluation Parameters of Oral Osmotic Drug Delivery System:

Evaluation of Powder:

- Weight of powder
- Bulk density
- Tapped density

- Carr’s index
- Angle of repose

Evaluation of Osmotic tablet:

- Hardness
- Thickness
- Friability
- Weight uniformity
- Stability Studies
- Effect of osmotic pressure
- Effect of pH on drug release
- Measurement of orifice diameter
- In vitro* drug release
- In vivo* Evaluation

TABLE 1: MARKETED PRODUCTS BASED ON OSMOTIC PRINCIPLES

Elementary osmotic pump (ALZA Corporation)	Once daily osmotic tablet with solid active agents	Push-pull osmotic delivery system (ALZA Corporation)	Multilayered tablet for drugs with low to high solubility
Efidac 24 [®]	Chlorpheniramine	Concerta [®]	Methylphenidate HCl
Volmax [®]	Albuterol	Covera HS [®]	Verapamil HCl
Acutrim [®]	Phenylpropanolamine	Glucotrol XL [®]	Glipizide
Sudafed 24 [®]	Pseudoephedrine	Ditropan XL [®]	Oxybutynin chloride

TABLE 2: HISTORICAL ASPECTS OF OSMOTIC PUMPS ²⁴

Year	Comments
1748	First report of osmosis
1877	Quantitative measurement of osmotic pressure
1955	First osmotic pump by Rose and Nelson
1973	Higuchi-leeper introduced a new version of Rose and Nelson pump with certain modifications
1973	Osmotically powdered agent dispense device with filling means
1975	Major milestone in the field of osmotic drug delivery introduced the first oral osmotic pump i.e. E.O.P
1976	Patent granted on the design of oral osmotic pump
1982	Patent issue for an osmotic system which consist of a layer of a fluid swell able hydro gel
1984	First report of combination therapy by use of push-pull osmotic pump
1985	Controlled porous osmotic pump was developed
1986	Patent issue claiming a delivery for controlled administration of drug to ruminants
1989	Developed push-pull osmotic pump for Nifedipine by Pfizer
1995	Patent to an osmotic dosage form for liquid drug delivery
1999	Asymmetric membrane capsule was introduced
2000	DUROS Leurpolid implants i.e. Viadur approved as first implantable osmotic pump for humans by US FDA
2001	Patent granted for dosage form comprising liquid drug formulation that can self emulsify to enhance the solubility, dissolution and bioavailability of drug
2003	First report osmotic floating system

CONCLUSION: In osmotic delivery systems, osmotic pressure delivers the driving force for drug release. Increasing pressure inside the device from water imbibition causes the drug to release from the

system. The major advantages include accurate control of zero-order or other patterned release over an extended time period—consistent release rates can be achieved irrespective of the environmental

factors at the delivery site. Controlled delivery through osmotic systems also reduce the side-effect profile by moderating the blood plasma peaks typical of conventional (e.g., instant release) dosage forms. Furthermore, since effective plasma levels are maintained longer in osmotic systems, avoidance of trough plasma levels over the dosing interval is possible. Though, a complex manufacturing process and higher cost compared with conventional dosage forms limit their use. Therefore, most of the currently marketed products are based on drugs used in long-term therapies for diabetes, hypertension, attention-deficit disorder, and other chronic disease states. Besides oral osmotic delivery systems, implants that work on osmotic principles are auspicious for delivery of a wide variety of molecules with a precise rate over a long period of time. Further, with the discovery of newer and potent drugs by the biotechnology industry, the need to deliver such compounds at a precise rate certainly will pave the way for osmotic delivery systems to play an increasingly important role in drug delivery.

REFERENCES:

- Ratnaparkhi, M. P. & Gupta, J. P. Sustained Release Oral Drug Delivery System - An Overview. *International Journal of Pharma Research & Review*. 2013; 2(3): 11-21.
- Khavarel NB, Dasankoppa F.S, Najundaswamy NG, A Review on Key Parameters and Components in Designing of Osmotic Controlled Oral Drug Delivery Systems. *Indian Journal of Novel Drug Delivery*, India. 2010; 2(4): 122-126.
- Gupta P.B, Thakur N, Jain N.P, Osmotically Controlled Drug Delivery System with Associated Drugs. *J Pharm Pharmaceutics Sci*, India. 2010; 13(3): 571-580.
- Aulton E.A, *Pharmaceutics The Science of Dosage form Design*, Churchill Livingstone, London, 417, 2002.
- Verma K.R, Krishna D. M, Garg S, Formulation aspects in the development of osmotically controlled oral drug delivery systems. *Elsevier*, India, 2002; 79: 7-27.
- Encyclopedia of Controlled Drug Delivery*, Volume 2 Copyright 1999 John Wiley & Sons, Canada 897-899
- Parashar B, Maurya B. Yadav V, Sharma L, A Review on Osmotically Regulated Devices. *The Pharma Innovation*, India. 2012; 1(4): 61-69.
- Gupta S, Singh R. P, Sharma R, Kalyanwat R, Lokwani P, Osmotic Pumps: A Review. *International Journal of Comprehensive Pharmacy*, India. 2011; 2(6):1-10
- Single D, Kumar SL. H, Nirmala, Osmotic Pump Drug Delivery: A Novel Approach. *International Journal of Research in Pharmacy and Chemistry*. 2012; 2(2): 661-670.
- Ghosh T, Ghosh A, Drug Delivery through Osmotic Systems – An Overview. *Journal of Applied Pharmaceutical Science*, India. 2011; 1(2): 38-49.
- Rathbone M.J., Hadgraft J., Roberts M.S. *Modified- Release Drug Delivery Technology*. Marcel Dekker, Inc. New York. 105. 2002.
- Jain N.K., *Pharmaceutical Product Development*. CBS Publishers & Distributors Pvt. Ltd., Noida, 105, 2006.
- Shokri J, Khosro A, Application of Cellulose and Cellulose Derivatives in Pharmaceutical Industries. *INTECH Open Science Open Minds*.2013;
- Panonummal HH R., Mathew V. *Controlled Drug Delivery System*. B. Pharm Projects and Review Articles Free download, India. 2009.
- Alli M., Senthil kumar S.K., Parthiban S, Review on Natural Pumps:A Novel Drug Delivery System. *International Journal of Pharmaceutical Development & Technology*. 2013; 3(2): 52-62.
- Types of osmotic pumps. Available at <http://www.pharmainfo.net/satyajeethpandey/blog/types-osmotic-pumps>. Accessed on (12-03-2013)
- Li X., Jasti B.R. *Design of Controlled Release Drug Delivery Systems*. McGraw- Hill. New York. 211, 227.
- Patel H, Patel U, Kadikar H, Bhimani B, Daslaniya D, Patel G, A Review on Osmotic Drug Delivery System. *International Research Journal of pharmacy*, India, 2012; 3(4): 88, 91
- Keraliya R. A, Patel C, Patel P, Keraliya V, Soni TG, Patel RC, Patel MM, Osmotic Drug Delivery Systemas a Part of Modified Release Dosage Form. *ISRN Pharmaceutics*, India. 2012; 1-9.
- Brindha S.V., et al (2012) Swellable Osmotic Drug Delivery System of Amitriptyline Hydrochloride – Design and Evaluation. *Journal of Current Chemical & Pharmaceutical Science*, India, 57.
- Patel K.N, Mehta T.A, A Review on Oral Osmotically Driven system. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2013; 5(3): 1005-1013.
- Thakor R.S, Majmudar F.D, Patel J. K, Rajput G. C, Patel M.P. Development and evaluation of osmotic drug delivery system for calcium channel blocker drug. *Scholars Research Library*, India.2010; 2(3): 43-51.
- Mothilal M, Damodharan N, Lakshmi K.S, Sharanya V, Srikrishna T. Formulation and In vitro Evaluation of Osmotic Drug Delivery System of Metoprolol Succinate. *International Journal of Pharmacy and Pharmaceutical Sciences*, India. 2010; 2(2): 64-68.
- Ratee P., Kumar V., Ahuja N. Osmotic-Controlled Release Oral Delivery System: An Advanced Oral Delivery Form. *ThaPharma Innovation*, 2012; 2(7): 116-124.

How to cite this article:

Khatri N, Nikam S and Bilandi A: Oral Osmotic Drug Delivery System: A Review. *Int J Pharm Sci Res* 2016; 7(6): 2302-12.doi: 10.13040/IJPSR.0975-8232.7(6).2302-12.