

OSMOTIC DRUG DELIVERY

CONTENTS: -

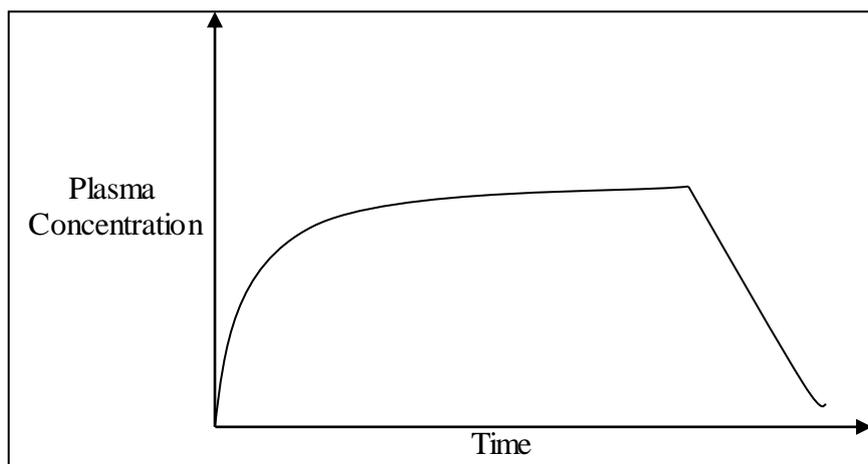
Sr. no.	Topics
1.	Introduction
2.	Definition
3.	Advantage of Osmotic DDS
4.	Disadvantage of Osmotic DDS
5.	Need for developing dosage form
6.	Mechanism of Osmosis
7.	Principle of Osmosis
8.	Factors affecting release of medicament from Osmotic DDS
9.	Formulation of Osmotic DDS
10.	Types of Osmotic pumps
11.	Evaluation
12.	Market products
13.	Questions
14.	References

1. INTRODUCTION

Controlled release dosage forms are designed to release drug in-vivo according to a predictable rate that can be verified by in-vitro measurement.

Potential development and new approaches to oral controlled release dosage forms include,

1. Hydrodynamic pressure controlled system
2. Intra-gastric floating tablet
3. Transmucosal tablet
4. Microporous membrane coated tablet.



Osmotic drug delivery has come a long way since Australian physiologists Rose and Nelson developed an implantable pump in 1955. Osmotic drug delivery uses the osmotic pressure for controlled delivery of drugs by using osmogens (for up to 10 – 16 hrs).

A) WHAT IS OSMOTIC PRESSURE

Osmotic pressure is a most important colligative property according to the pharmaceutical point of view. Colligative property is the concentration of solution independent of solute property.

Osmotic pressure of a solution is the external pressure that must be applied to the solution in order to prevent it from being diluted by the entry of solvent via a process known as osmosis.

Such a membrane is only permeable to solvent molecules. Because only solvent can pass through the semi-permeable membrane, the driving force for the osmosis arises from the inequality of the chemical potentials of the solvent on opposing sides of the membrane.

B) WHERE IT IS USE IN PHARMA

For adjustment
tonicity in

- Parenteral
- Ophthalmic

For developing Osmotic
drug delivery system

For Oral use in of
treatment of

- Constipation
- Hypertension

2. DEFINITION

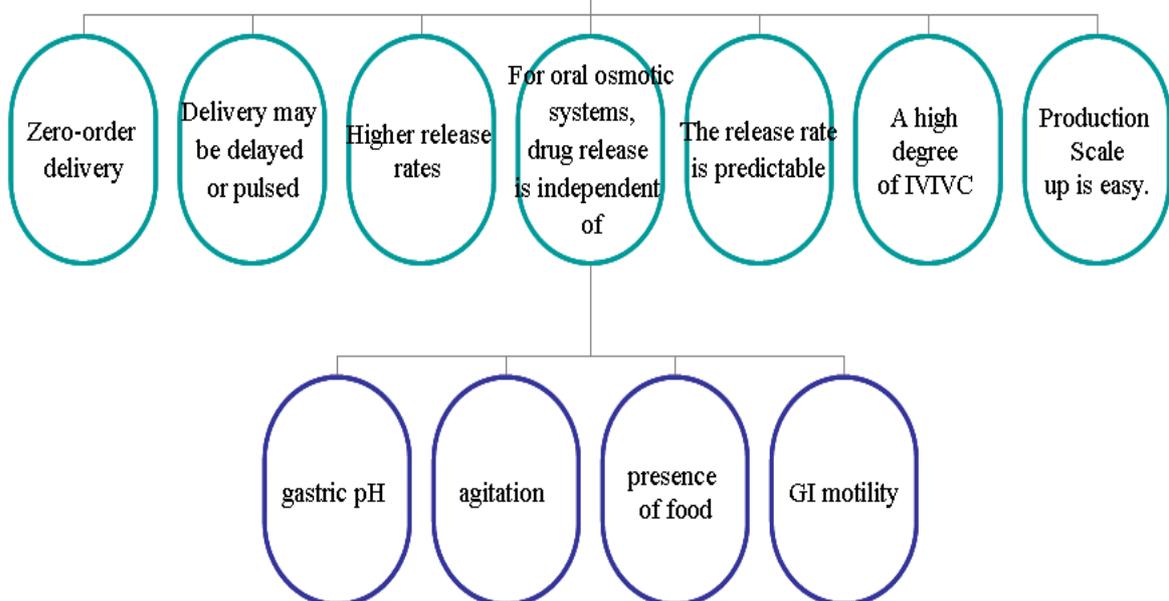
Osmolality is the number of osmoles per Kg of water.

Osmolarity is the number of osmoles per liter of solution.

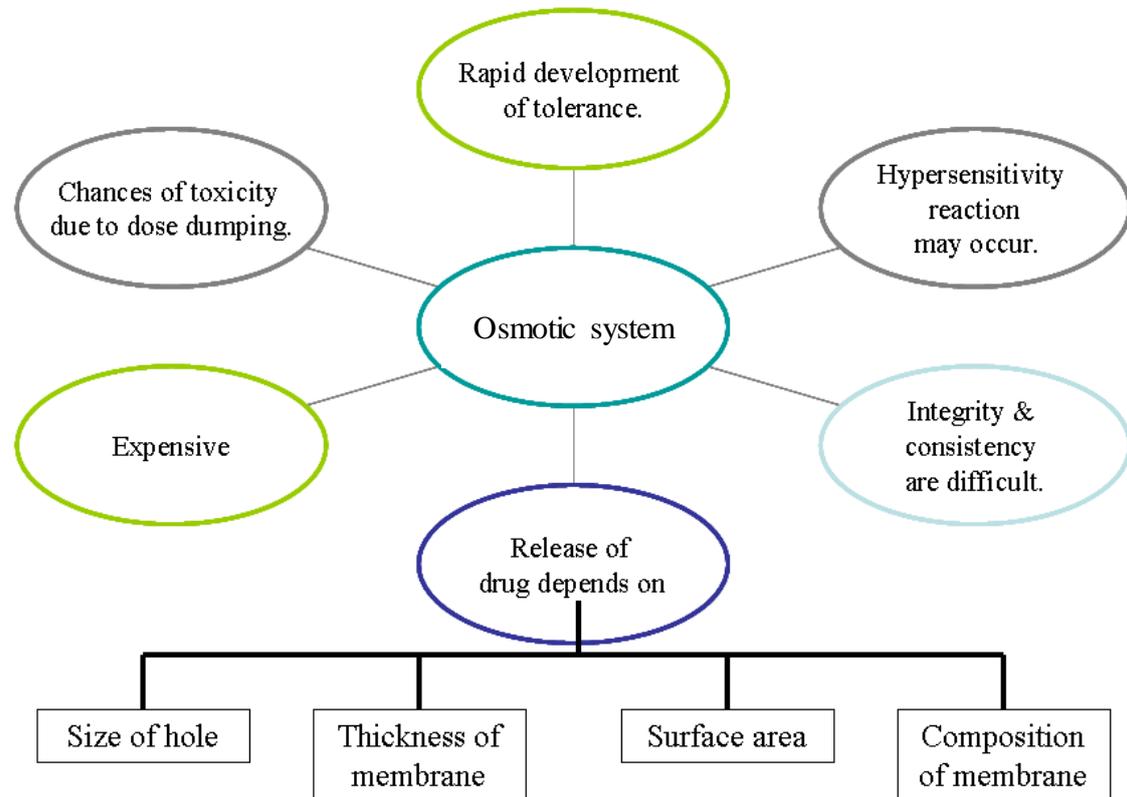
Iso-osmotic solution is one where two solution are separated by a perfect semi permeable membrane (SPM is membrane which is permeable only to solvent molecule and no net movement of solute occur across the membrane.

In **Isotonic** solution biological membrane do not always function as perfect SPM and some solute molecule as well as water are able to pass through them.

3. ADVANTAGE OF OSMOTIC DDS



4. DISADVANTAGE OF OSMOTIC DDS



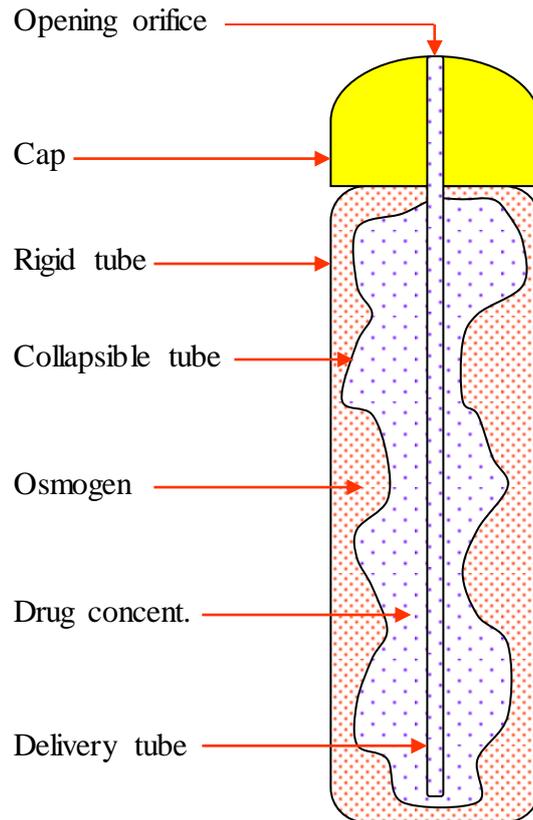
5. NEED FOR DEVELOPING DOSAGE FORM

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

6. MECHANISM OF OSMOSIS

Core contains water soluble osmotically active agent and blended with water soluble or insoluble drug, additives and coating has been carried out which functions as a semi permeable membrane.

Since barrier is only permeable to water, initial penetration of water dissolves the critical part of the core, resulting in development of an osmotic pressure difference across the membrane.



The device delivers a saturated volume equal to the volume of water uptake through the membrane. Initial lag time (per hour) during which delivery rate increases to its maximum value, drug release is zero order, until all solid material is dissolved.

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

$$\Pi V = n_2 RT$$

Where V = is the volume of solution.

n_2 = is number of moles of solute.

T = thermodynamic temperature and

R = is the gas constant.

7. PRINCIPLE OF OSMOSIS

The solvent membrane control delivery of agent from the osmotic system across the semi permeable membrane, which in turn drive the agent out. Water influx of osmotic pump can be describe as,

$$\frac{dv}{dt} = \frac{A}{h} LP \sigma (\Delta\Pi - \Delta P)$$

Where $\frac{dV}{dt}$ = Water influx

dt

A = Membrane area

h = Membrane thickness

P = Mechanical permeability

$\Delta\Pi$ = Osmotic pressure

ΔP = Hydrostatic pressure difference between inside and outside the system

The general expression for the solute delivery rate, dM / dt obtained by pumping through the orifice of the reservoir is given by,

$$\frac{dM}{dt} = \frac{dV}{dt} C$$

Where C = concentration of solute if dispersed fluid

σ describes the leakages of solute through the membrane. A perfect semi permeable membrane is selectively permeable to water only and does not allow solute to pass through it (σ is close to unity). By substituting the product of LP σ with membrane permeability k, equation becomes,

$$\frac{dM}{dt} = \frac{A}{h} k \Pi C$$

It is possible to obtain constant zero order release rate from osmotic system by maintaining the terms on right side of equation constant. As long as the excess solid osmotic agent is present inside the system both Π and C can be maintained at constant level corresponding to the saturated solution of agent.

Above equation describe to all osmotically driver system including EOP and the agent reservoir (Alzet osmotic pumps). Here drug release also take place via, i.e drug release is describe by equation combining osmosis and diffusion component.

The diffusion component is added because the membrane used is not perfectly semi permeable in nature and thus a portion of drug is released by diffusion permeability through the pores in the coating. The total mass delivery dM / dT per unit time is given by,

$$\left(\frac{dM}{dT} \right)_t = \left(\frac{dM}{dT} \right)_o + \left(\frac{dM}{dT} \right)_d$$

Where mass released by pumping and diffusion respectively and osmotic release component is given by,

$$\left(\frac{dM}{dT} \right)_d = P_d A C / h$$

Where P_d = dissolved drug permeability.

The push pull osmotic pump consists of two compartments and is coated with a semi permeable membrane. Drug along the osmotic agent is present in upper compartment, whereas lower compartment consist of osmotic agent. The drug compartment is connecting to outside environment via delivery orifice. After coming in contact with aqueous environment, imbibitions of fluid by the drug compartment take place to form the fluid composition that is delivered by the delivery orifice. Simultaneously imbibition of fluid by the push compartment causes it to swell and co-operate with the drug composition for delivering the drug from delivery orifice.

The mass delivery from the push pull osmotic pump is given by,

$$dM / dT = (Q + F) F_d C_0$$

Q and F are osmotic flow in the osmotic and drug compartment respectively. F_d is the fraction of drug formulated in drug compartment. C_0 is the concentration of solid dispersion.

8. FACTORS AFFECTING RELEASE OF MEDICAMENT

Factors affecting the release rate of medicament from osmotic drug delivery system are,

1. Solubility
2. Osmotic pressure
3. Delivery orifice
4. Membrane type

A) SOLUBILITY

Solubility of drug is one of the most important factors since kinetic of osmotic release is directly related to the drug solubility.

The fraction of a drug release with zero order kinetic is given by

$$F(z) = 1 - \frac{S}{P}$$

Where $F(z)$ = fraction release by zero order

S = drug solubility in g / cm^3

P = density of core tablet.

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

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

B) OSMOTIC PRESSURE

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

$$\frac{dM}{dt} = \frac{A k \Pi C}{h}$$

In order to achieve optimized and constant Osmotic Pressure in compartment Osmotic agent must be added to tablet

Sr. no.	Osmogen	Osmotic Pressure
1.	NaCl	356
2.	Fructose	355
3.	KCl	345
4.	Sucrose	150
5.	Xylitol	104
6.	Sorbitol	84
7.	Dextrose	82
8.	Citric acid	69
9.	Tartaric acid	67

So varying the osmogen vary osmotic pressure and hence drug release. Osmogen are classified as inorganic and organic osmogens.

Sr. no	Combined osmogen	Osmotic Pressure
1.	Lactose – Fructose	500
2.	Dextrose – Fructose	450
3.	Sucrose – Fructose	430
4.	Mannose – Fructose	415
5.	Lactose – Sucrose	250
6.	Lactose – Dextrose	225
7.	Mannose - Lactose	225

C) DELIVERY ORIFICE

Formation of orifice can take place by,

- Laser,
- Microdrill,
- Modified punches,
- Controlled porosity osmotic pumps can be generated by in-situ formation of delivery orifice which has been described in US Patent.

In case of Propranolol HCL Oral Osmotic Tablet,

1. Tablet with orifice diameter of 200 – 800 μm showed zero order release and
2. The same with 1 mm orifice diameter showed abnormal release.

So in fact orifice diameter should be below A_{max} and should be greater than A_{min} since in vivo drug tablet will swell and still minimise the bore. So uneven and unpredictable release will occur.

For delivery containing KCl, orifice should be between 75 to 275 microns in diameter.

D) MEMBRANE TYPE

Drug release from osmotic system is largely independent of pH and agitational intensity of GIT

Example are Cellulose Ester, Cellulose Triacetate, Cellulose Propionate, Cellulose Acetate Butyrate, Ester, Ethyl Cellulose and Eudragits.

Among above Cellulose Acetate Butyrate is most commonly used since of its,

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

SPM	WVTR (g/100m ² /24hr/mmthick)
PVA	100
Methyl cellulose	70
Cellulose acetate	40-75
Ethyl cellulose	75
Ethylene vinyl acetate	1-3
Cellophane	>1.2

However asymmetric membrane capsule are new type of coating which can be fully utilized for osmotic drug delivery system and offers significant advantage over membrane coating used in conventional Osmotic DDS which devoid of coating defects and they are having higher rate of water influx which allow the release of drug with lower or no osmotic pressure or lower solubility.

9. FORMULATION OF OSMOTIC DDS

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

A) DRUG

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

B) SEMIPERMEABLE MEMBRANE

Semipermeable membrane must possess certain performance criteria:

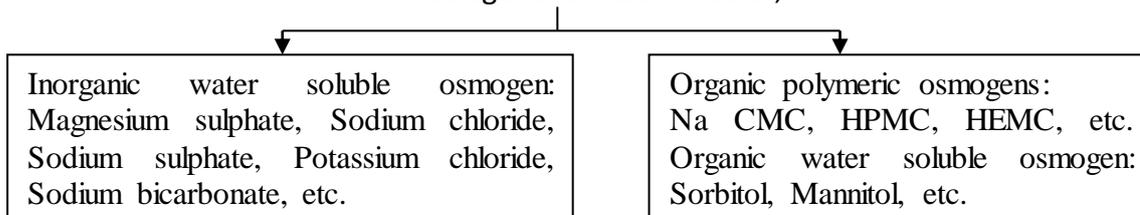
- It must have sufficient wet strength and water permeability.
- It should be selectively permeable to water and biocompatible.

Some other polymers such as agar acetate, amylose triacetate, betaglukan acetate, poly (vinylmethyl) ether copolymers, poly (orthoesters), poly acetals, poly (glycolic acid) and poly (lactic acid) derivatives.

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

C) OSMOGEN / OSMAGENT / OSMOTIC DRIVING AGENT

Osmotic agents are classified as,



D) HYDROPHILIC AND HYDROBHOBC POLYMERS

These polymers are used in the formulation development of osmotic systems containing matrix core.

The selection of polymer is based on the solubility of drug as well as the amount and rate of drug to be released from the pump.

The highly water soluble compounds can be co-entrapped in hydrophobic matrices and moderately water soluble compounds can be co-entrapped in hydrophilic matrices to obtain more controlled release.

Examples of hydrophilic polymers are hydroxy ethyl cellulose, carboxy methyl cellulose, hydroxyl propyl methyl cellulose, etc.

Examples of hydrophobic polymers are ethyl cellulose, wax materials, etc.

E) WICKING AGENTS

It is defined as a material with the ability to draw water into the porous network of a delivery device.

The function of the wicking agent is to draw water to surfaces inside the core of the tablet, thereby creating channels or a network of increased surface area.

Examples are colloidon silicon dioxide, kaolin, titanium dioxide, alumina, niacinamide, sodium lauryl sulphate (SLS), low molecular weight polyvinyl pyrrolidone (PVP), bentonite, magnesium aluminium silicate, polyester and polyethylene, etc.

F) SOLUBILIZING AGENTS

Non swellable solubilizing agents are classified into three groups

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

G) SURFACTANTS

They are added to wall forming agents.

They act by regulating the surface energy of materials to improve their blending in to the composite and maintain their integrity in the environment of use during the drug release period.

Examples: polyoxyethylenated glyceryl recinoleate, polyoxyethylenated castor oil having ethylene oxide, glyceryl laurates, etc.

H) COATING SOLVENTS

Solvents suitable for making polymeric solution that is used for manufacturing the wall of the osmotic device include inert inorganic and organic solvents.

Examples: methylene chloride, acetone, methanol, ethanol, isopropyl alcohol, ethyl acetate, cyclohexane, etc.

I) PLASTICIZERS

Permeability of membranes can be increased by adding plasticizer, which increases the water diffusion coefficient.

Examples: dialkyl phthalates, trioctyl phosphates, alkyl adipates, triethyl citrate and other citrates, propionates, glycolates, glycerolates, myristates, benzoates, sulphonamides and halogenated phenyls.

J) FLUX REGULATORS

Flux regulating agents or flux enhancing agent or flux decreasing agent are added to the wall forming material; it assist in regulating the fluid permeability through membrane.

Poly hydric alcohols such as poly alkylene glycols and low molecular weight glycols such as poly propylene, poly butylene and poly amylene,etc. can be added as flux regulators.

K) PORE FORMING AGENTS

These agents are particularly used in the pumps developed for poorly water soluble drug and in the development of controlled porosity or multiparticulate osmotic pumps.

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

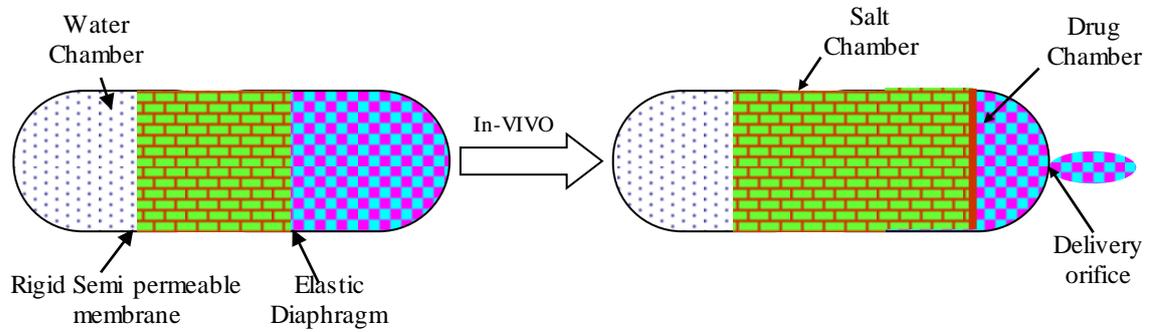
Like,

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

10. TYPES OF OSMOTIC PUMPS

A) IMPLANTABLE OSMOTIC PUMPS

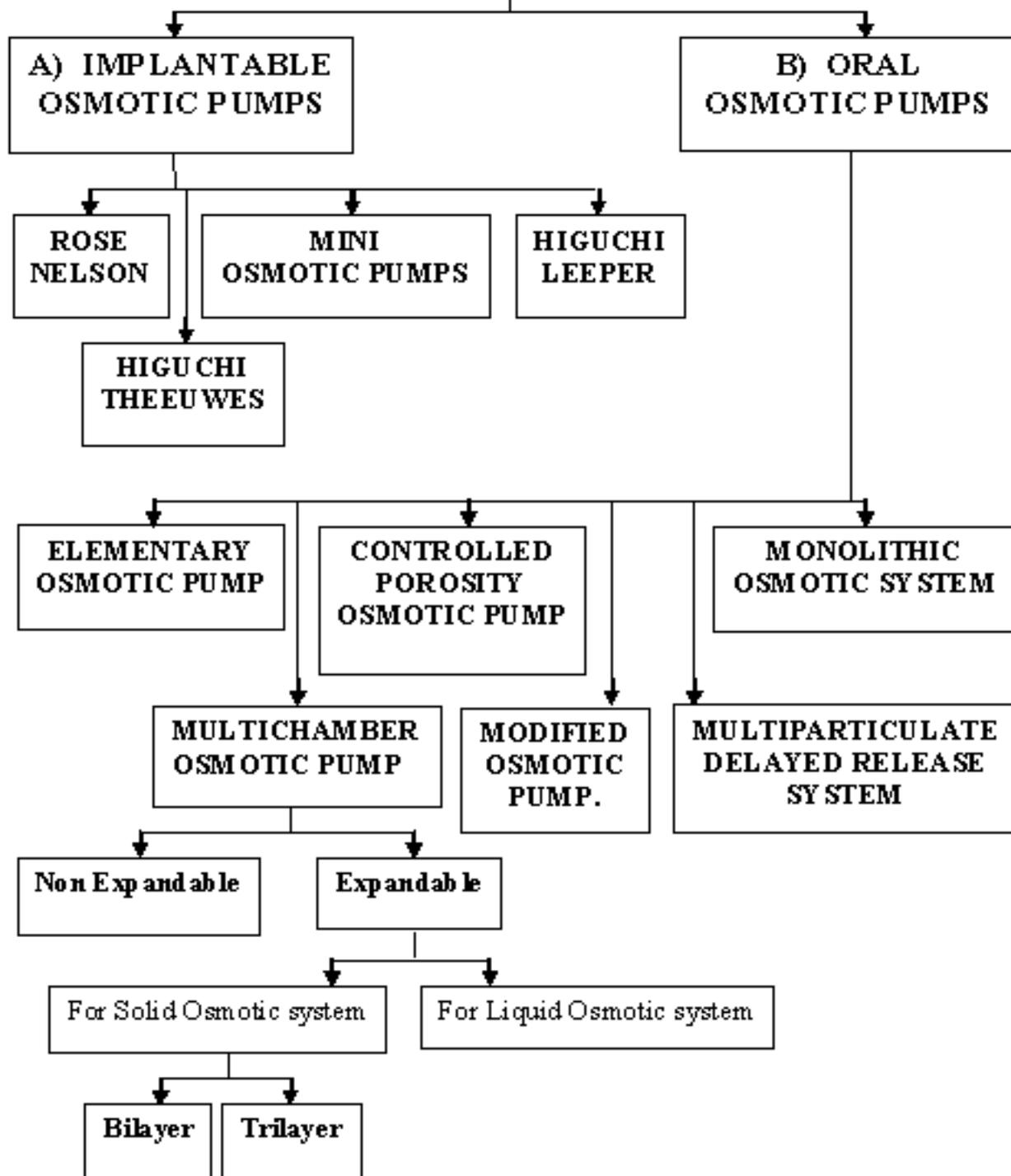
I) ROSE-NELSON OSMOTIC PUMP



Rose and Nelson developed the first osmotic pump in 1955.

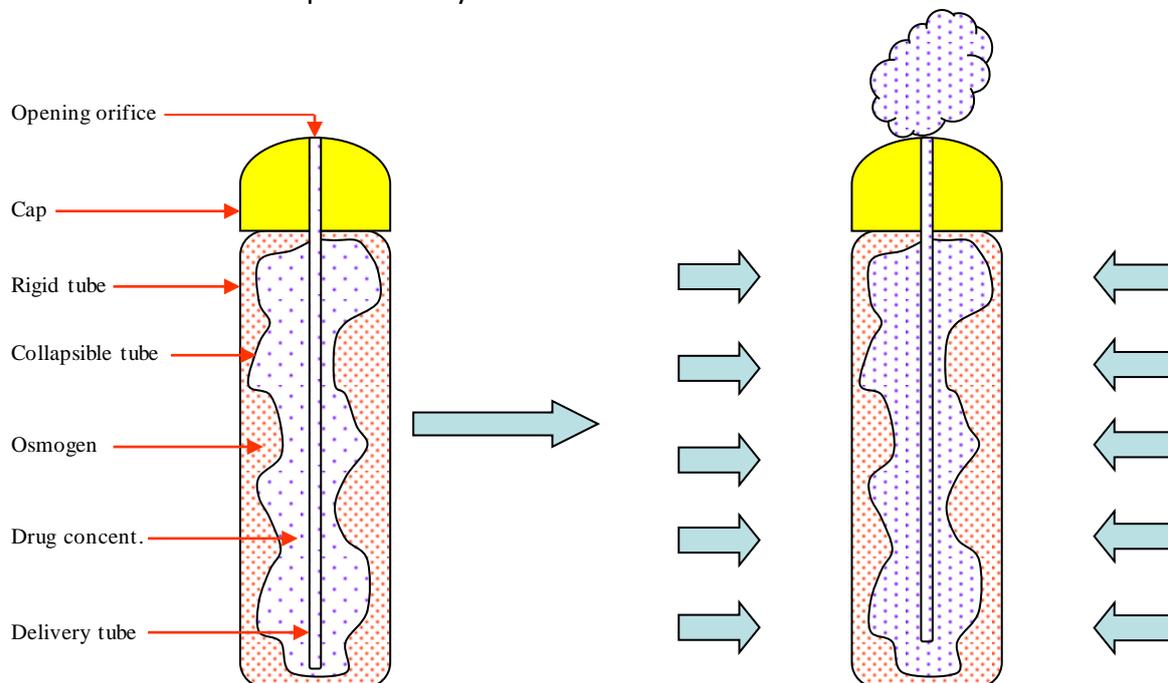
The Osmotic pump was having three chambers. Water to be loaded prior to use was the drawbacks of rose nelson osmotic pump.

CLASSIFICATION OF OSMOTIC PUMPS



II) HIGUCHI THEEUWES OSMOTIC PUMP

The release of the drug from the device is governed by the salt used in the salt chamber and the permeability characteristics of outer membrane.



Diffusional loss of the drug from the device is minimized by making the delivery port in shape of a long thin tube.

In this device, the rigid housing is consisted of a semi permeable membrane. The drug is loaded in the device only prior to its application, which extends advantage for storage of the device for longer duration.

When pump placed in an aqueous environment a saturated solution of drug is developed since Semi permeable membrane draws water inside pump which generate osmotic pressure. This pressure is relieved by the flow of saturated solution out of device through the delivery orifice. This process continue at a constant rate untill the entire solid drug inside the pump has been dissolved and at last only a solution filled shell remains.

Small osmotic pumps of this form are available under the trade name Alzet®.

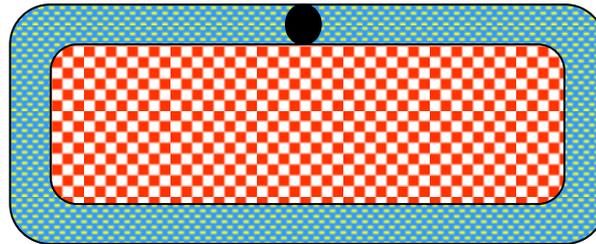
Delivery of DNA by agarose hydrogel implant facilitates genetic immunization in cattle by using Alzet osmotic pumps.

B) ORAL OSMOTIC PUMPS

I) ELEMENTARY OSMOTIC PUMP

Rose Nelson pump was further simplified in the form of elementary osmotic pump by Theeuwes in 1975.

By Higuchi and Theeuwes pump by elimination the separate saturated chamber and using the drug itself as the osmotic agent.



It is fabricated as a tablet coated with SPM

When tablet placed in an aqueous environment a saturated solution of drug is developed since Semi permeable membrane draws water inside tablet which generate osmotic pressure. This pressure is relieved by the flow of saturated solution out of device through the delivery orifice. This process continue at a constant rate untill the entire solid drug inside the tablet has been dissolved and at last only a solution filled shell remains.

Normally EOP deliver 60 – 80 % of its content at constant rate.

It has short lag time of 30 – 60 minute.

LIMITATION: -

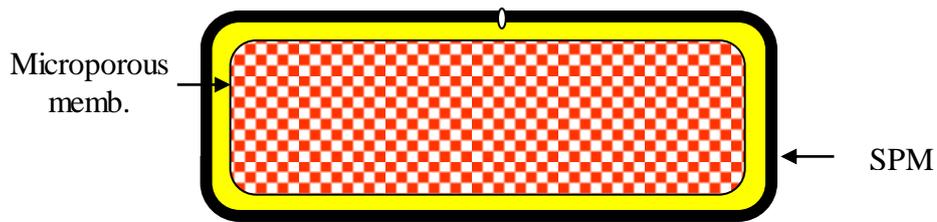
- SPM should be 200-300 μ m thick to withstand pressure
- Thick coatings lowers the water permeation rate
- Applicable mostly for water soluble drugs

II) MODIFIED OSMOTIC PUMP

a) Osmotic Pumps for Moderately Soluble Drugs

Semi permeable membrane must be 200-300 microns thick to withstand the pressure generated within the device.

These thick membranes lowers water permeation rate, which is not desirable for moderately soluble drugs.



 Drug and osmogen

This problem can be overcome by using coating materials with high water permeability. For example, addition of plasticizers and water soluble additive to the cellulose acetate membranes, this increased the permeability of membrane up to ten fold.

Composite structured semi permeable membrane is used for moderately soluble drugs.

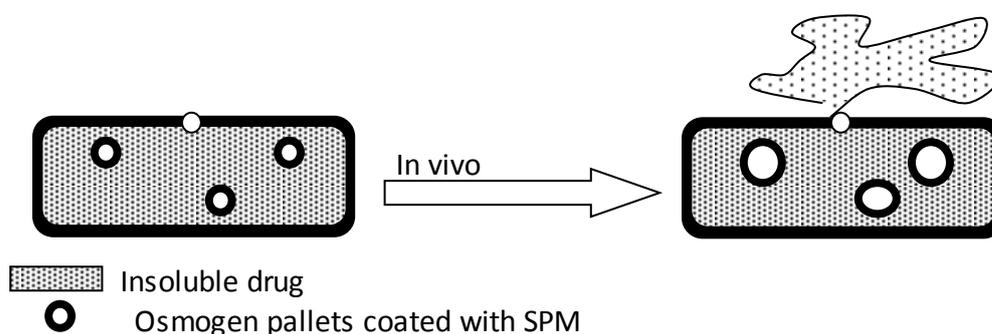
The first layer is made up of thick micro porous film that provides the strength required to withstand the internal pressure, while second layer is composed of thin semi permeable membrane that produces the osmotic flux.

The support layer is formed by, Cellulose acetate coating containing 40 to 60% of pore forming agent such as Sorbitol.

b) Osmotic Pump for Insoluble Drugs

Osmotic agents are coated with an elastic semi permeable membrane film in fluid bed coater and this particle are then mixed with insoluble drugs and compressed to form tablet which is coated with SPM and orifice is created in membrane.

After coming in contact with aqueous environment, water is drawn through the two membranes into the osmotic agent particle which swells and hydrostatically pushes the insoluble drug via the orifice.



III) MULTICHAMBER OSMOTIC PUMP

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

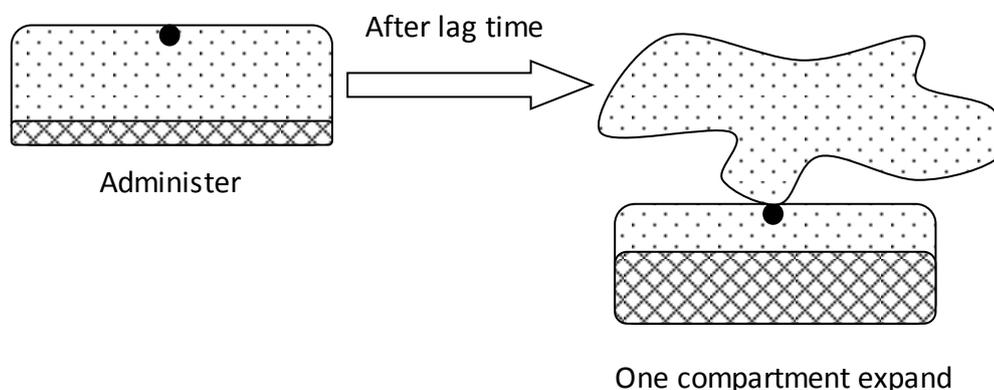
There are two type of MOP

a) Expandable

i) For Solid Osmotic System

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

Example ProcardiaXL for Nifedipine

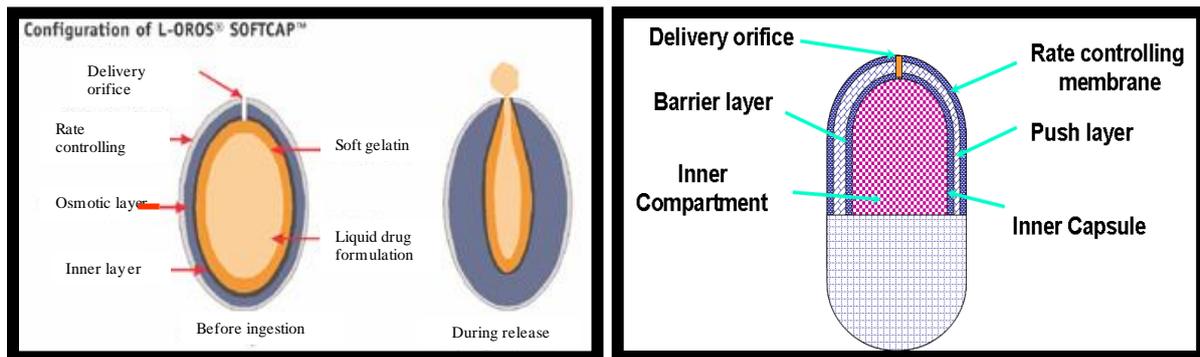


When PPOP come in contact with an aqueous environment both drug layer and polymer imbibe water. As lower compartment is devoid of any orifice it expands and pushes the diaphragm into the upper chamber and hence deliver drug via orifice.

Another variation on the Push-Pull system, the capsule-shaped tablet, makes possible patterned delivery (ascending or pulsed delivery) of one or more drugs. The capsule shaped tablet consists of the multicompartament core, semipermeable membrane and a delivery orifice of the basic Push-Pull system and uses the same osmotic principles, but the capsule shape allows more versatility in patterned delivery.

ii) For Liquid Osmotic System

A liquid formulation is use for delivering insoluble drugs and macromolecules. Such molecules require external liquid components to assist in solubilization, dispersion, protection from enzymatic degradation and promotion of gastrointestinal absorption. Thus the L-OROS system was designed for continuous delivery of liquid drug.



One type of L-Oros system consists of a soft gelatin capsule (softcap™) surrounded by a barrier layer, an osmotic push layer, and a semipermeable membrane. As with other Oros system, drug is released through a delivery orifice in the semipermeable membrane.

Another type of L-Oros system consists of a hard gelatin capsule (Hardcap™) containing a liquid drug layer, a barrier layer, and a push layer surrounded by a semipermeable membrane. The L-Oros Hardcap system was designed to accommodate more viscous suspensions with higher drug loading than would be possible with Softcap design.

b) Non Expandable

Non expandable osmotic pump maintains the volume throughout the period of operation means the rigid one

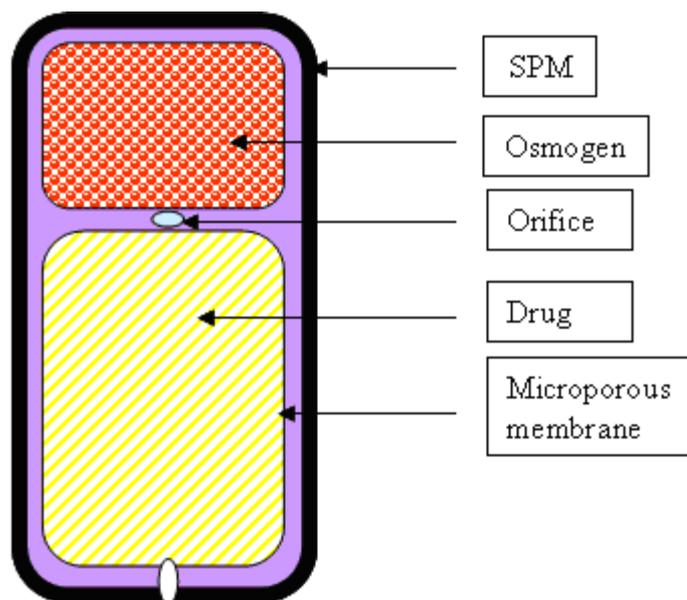
Depending on function of second chamber non-expandable osmotic pump are divided into two subtypes,

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

Such is useful when saturated solution of drug irritate GIT.

ii) Two separate EOP tablet formed in single tablet

Here one chamber contains osmogen and second chamber contain drug. When such system comes in contact with aqueous environment, solution of osmotic agent formed in first chamber is delivered to drug chamber via the concentric hole, where it mixes with drug solution before coming out of the micro porous membrane that forms the pores of SPM surrounding the drug chamber useful for insoluble drug delivery.



IV) CONTROLLED POROSITY OSMOTIC PUMP

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



Some of the pores forming additives that can be used are NaCl, KCl, and Urea. The rate of release from Controlled Porosity Osmotic Pump has been reported to be dependent on the coating thickness, level of soluble component in coating, solubility of drug in tablet core and osmotic pump diffuses across the membrane.

The rate of release from controlled porosity osmotic pump is dependent on

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

Drug release from the whole surface of device rather than from a single hole which may reduce stomach irritation problem.

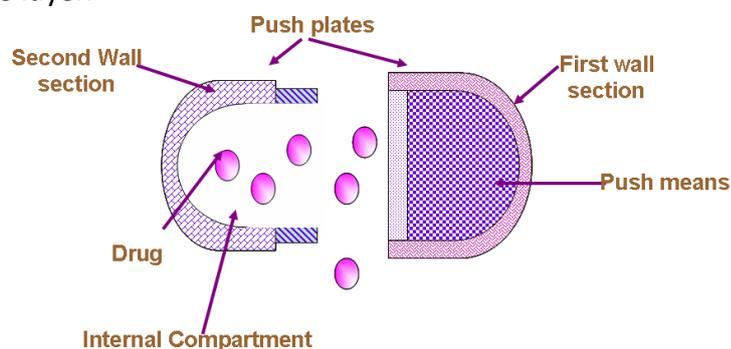
Hole is produce by the coating procedure hence complicated laser drilling is not required.

Citric acid is used as a pore-forming agent in chitosan-based colon-specific pumps.

V) MULTIPARTICULATE DELAYED RELEASE SYSTEM

Pellets containing drug with or without osmotic agent are coated with a semi-permeable membrane which, on contact with an aqueous environment, results in the penetration of water into the core and forms a saturated solution of the soluble component. The osmotic pressure difference results in the rapid expansion of the membrane, which leads to the formation of pores.

For controlled release, drug is located at the first orifice, and for fast release, a drug layer is located adjacent to the second orifice. A push layer is located between the controlled and fast release layers.



The dispenser comprises a housing that has first- and second-wall sections in a slideable telescoping arrangement.

The housing maintains integrity in its environment of use.

The device consists of two chambers; the first contains the drug and an exit port, and the second contains an osmotic engine. A layer of wax-like material separates the two sections.

To assemble the delivery device, the desired active agent is placed into one of the sections by manual- or automated-fill mechanisms.

The bilayer tablet with the osmotic engine is placed into a completed cap part of the capsule with the convex osmotic layer pointed into the closed end of the cap and the barrier layer exposed toward the cap opening. The open end of the filled vessel is fitted inside the open end of the cap, and the two pieces are compressed together until the cap, osmotic bilayer tablet, and vessel fit together tightly.

As fluid is imbibed through the housing of the dispensing device, the osmotic engine expands and exerts pressure on the slideable connected first and second wall sections.

During the delay period, the volume of the reservoir containing the active agent is kept constant; therefore, a negligible pressure gradient exists between the environment of use and the interior of the reservoir. As a result, the net flow of environmental fluid driven by the pressure to enter the reservoir is minimal, and consequently no agent is delivered for the period.

VI) MONOLITHIC OSMOTIC SYSTEM

Dispersion of water soluble drug is made in a polymeric matrix and compressed as tablet.

Tablet is then coated with semi permeable membrane or drilled on both side of tablet.

When MOS comes in contact with aqueous environment, the water penetrates in the core and forms a saturated solution of component which will generate osmotic pressure which results in the rupturing of membrane of polymeric matrix surrounding the agent. Thus liberating drug to move outside the environment.

MOS is simple to prepare but the system fails if more than 20 – 30 % volume of active agent is incorporated in device because above this level significant contribution is from leaching of substance

Ketoprofen Monolithic Osmotic Pump Control Release Tablet made up of PEG 6000, NaCl, CMC-Na and Polyvinyl pyrrolidone which releases drug at 93.51 % for 24 hrs

11. EVALUATION

A) WEIGHT VARIATION

B) HARDNESS

C) FRIABILITY

D) THICKNESS

E) DISSOLUTION

F) PORE DIAMETER

G) COATING THICKNESS

H) IN VITRO EVALUATION

The in vitro release of drugs from oral osmotic systems has been evaluated by the conventional USP paddle and basket type apparatus.

The dissolution medium is generally distilled water as well as simulated gastric fluid (for first 2-4 h) and intestinal fluids (for subsequent hours) have been used.

The standard specifications, which are followed for the oral controlled drug delivery systems are equivalently applicable for oral osmotic pumps.

I) IN VIVO EVALUATION

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

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

12. MARKET PRODUCTS

Sr. no	Product	Drug	Manufacturer
1.	Osmosin	Indomethacine	Merck / Alza
2.	Procardia	Nifedipine	Pfizer / Alza
3.	Cyclobenzaprine OROS	Cyclobenzaprine	Merck / Alza
4.	Efidac 24	Chlorpheniramine maleate	Novartis / Pfizer / Alza
5.	Glucotrol XL	Glipizide	Pfizer / Alza
6.	Minipress XL	Prazocin	Pfizer / Alza

13. QUESTIONS

1. What is ODDS? Why it is required? Enumerate recent advance in controlled osmotic drug delivery system with their approaches.
2. What are ideal properties of semi permeable membrane? Suggest few materials for this. Write note on evaluation of osmotic pump.
3. Write a note on principle of osmotic drug delivery system.
4. Give advantage and disadvantage of osmotic drug delivery system.
5. Give name of osmotic pumps. Give detail on elementary osmotic pump.

14. REFERENCES

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