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A COMPLETE RECAPITULATION OF A DRUG DELIVERY BASED ON OSMOTIC PRESSURE: AN OSMOTIC DRUG DELIVERY SYSTEM

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Implantable devices, Oral osmotic device, Osmogents, Osmotic pressure, Drug delivery orifice, Semipermeable membrane, Pumping devices, Push & Pull layers.

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ABSTRACT: Conventional dosage forms are the systems that don't have complete control on their drug release, and also there is no control over the effective concentration at the target site. So in order to overcome this problem the osmotic drug delivery system was developed for the controlled delivery of drugs. This osmotic drug delivery system includes dosage forms for oral administration and implantable systems where they provide controlled delivery of drugs. These systems contain osmotic agents and a semipermeable membrane where they play an important role in the development of these delivery systems. This review mainly concentrates on the main Advantages, the principle of osmosis and how the drugs are delivered by using osmotic pressure, historical background, Types of osmotic drug delivery - Implantable and oral osmotic system, their pictorial representations and mechanisms, factors influencing the drug release, scientific developments and Marketed products of osmotic drug delivery systems.

INTRODUCTION: Oral drug delivery is one of the oldest and most widely used routes for the administration of drugs for achieving local and systemic effects. In this, the conventional dosage forms are able to give an immediate release of drugs but they are unable to control the drug release and they cannot maintain effective concentration at the target site for a longer period of time. In turn, the bioavailability of drugs purely depends on the physicochemical properties of a drug, excipients, and many physiological factors [1,2].

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Due to all these limitations of the conventional dosage form, researchers have concentrated on developing novel drug delivery systems (NDDS), which is a key area of (FR&D) pharmaceutical research and development. This NDDS controlled release drug delivery system has gained more importance because of its many advantages than conventional dosage forms.

Controlled release drugs are easy to administer, have better patient compliance and decrease dosing frequency where the main goal of controlled release drug delivery is to improve the efficacy of drugs by prolonging the drug release for an extended period of time [3]. In this novel drug delivery system, the drug release can be regulated by preparing them in different ways such as matrix system, reservoir system and osmotic systems. Where the osmotic drug delivery Systems are more

well-founded controlled release drug delivery systems, which can be administered orally [4]. Here in this osmotic drug delivery system, osmotic pressure is used as a driving force to release the drug in a controlled manner [5]. Drug release from this system is independent of pH and other physiological parameters [6]. There are many advantages of osmotically controlled drug delivery systems given in the following **Table 1**. Osmotic drug delivery systems have many benefits practically when compared to conventional dosage forms. Whereas they also have some disadvantages. Some distinct advantages and disadvantages of Osmotic drug delivery systems are as follows.

TABLE 1: ADVANTAGES AND DISADVANTAGES OF OSMOTICALLY DRUG DELIVERY SYSTEMS [7, 14]

Advantages [7–12]	Disadvantages [13–14]
The mechanism of drug release is independent of drug concentration	High care should be taken for the coating process because coating film defects may result in dose dumping
Drug delivery may be delayed or sometimes even pulsed if required	Highly expensive due to specialized equipment
Increases the bioavailability of drugs	Requires inert ingredients for the preparation of osmotic tablets
Sustained blood levels within the therapeutic window	Drug delivery orifice making is the critical step in osmotic tablets preparation
Inter and intra subject variability is less	Osmotic drug delivery systems cannot be crushed or chewed
Drug delivery is independent of outside agitations, gastric pH, hydrodynamic conditions and even GI motility	Drug release may be affected in the presence of food to some extent
Drug release rate is highly predictable	Drug retrieval is not possible in case of adverse effects.
Better *in vitro-in vivo* correlation (IVIVC) with specific limits	Rapid development of tolerance
Safety margin for high potency drugs	
Able to produce better release rates than conventional dosage forms	
Extremely useful for patients suffering	
Enhanced patient compliance	
Drug release can be programmable	
They can be well characterized	
Less or reduced side effects	
Gives zero-order release profile after lag time	

Limitations: Moreover, in addition to these, there are certain limitations associated with these osmotic drug delivery systems they are.

- They may cause ulcers due to the release of a saturated solution.
- Extraordinary systems are necessary for making orifices to the device, resulting in an increase in making costs.
- Experienced personnels are required for the production of these osmotic drug delivery devices.
- Residence time of the osmotic drug delivery system in the body may vary with gastric motility and after eating food.

Historical Background [14, 22]: In the year 1955, two scientists Rose and Nelson used osmosis principle for the first time in drug delivery systems and they have developed an implantable pump that consists of three chambers. In 1970's Higuchi and Leeper developed and proposed a series of variations in the Rose and Nelson pump. Then in 1974, the scientist Theeuwes developed the first osmotic drug delivery concept; also he simplified the Rose-Nelson pump which was developed by Alza Corporation of the USA and also he developed an elementary osmotic pump and holds several patents and released many osmotic drug delivery system products in the market.

Later the Rose-Nelson pump was further simplified and developed by Higuchi and Theeuwes. And also, they have designed a tablet that contains a core surrounded by a semipermeable membrane that contains an orifice. In the 1980's the first two osmotic drug delivery products were released into the market; they are indomethacin, Osmosin and phenylpropanolamine. Osmosin, which is an elementary osmotic pump, was withdrawn from the market due to its large number of side effects.

Zentner *et al.* in 1985-1991, Zentner and Rork in 1990, Appel and Zentner and Mcclelland *et al*. In 1991, they developed a controlled-porosity osmotic pump tablet as an oral drug delivery system. Later oral osmotic drug delivery system was further developed with two new designs one delivered 0.02 ml/day for 100 days and the other delivered 0.5 ml/ day for 4 days, both are used in pharmacological research, they are push-pull osmotic pumps (PPOP) it was developed for the application of poorly water soluble drugs to the targeted site and controlled-porosity osmotic pumps (CPOP) was developed to decrease the risk of drug induced irritation.

Osmosis & ITS Principle [23, 25]: Osmosis is a process by which molecules of a solvent tend to pass through a semipermeable membrane from a low concentrated solution into a highly concentrated one. This osmosis process is able to control drug delivery. This type of osmotic drug delivery device contains osmogent, due to which osmotic pressure is created. (The osmotic pressure of a solution is the external pressure applied to the solution to prevent it from being diluted by the entry of solvent *via* the osmosis process. So that when this device comes in contact with fluids, osmotic pressure is created, due to high osmotic pressure inside the device, the drug pushes outside.

Moreover the release rate of the drugs from osmotic drug delivery devices depends on molecular weight, solubility and activity coefficient of the solute (osmogent). According to the Pfeffer experiment, it was reported that the membrane is permeable to water but the membrane-impermeable to sugars is used to separate a sugar solution from the pure water. He showed that the osmotic pressure π of the sugar solution is directly proportional to the concentration of the solution and absolute temperature. Later within a few years, Van't Hoff shows the comparison between these results and ideal gas law with the following equation.

π = Φ c r t Where, π = Osmotic pressure. Φ = Osmotic coefficient of the solution. C = Molar concentration of sugar in the solution. r = Gas constant t = Absolute temperature

Osmotic pressure for the concentrated solution of soluble solutes commonly used for controlled release formulation; their osmotic pressure can produce high water flow across the semipermeable membrane. The osmotic water flows through a membrane is given by equation.

Dv/dt = A Q Δ π/ Where, dv\dt = Water flows across the membrane. A = Area. L = Thickness. **Δπ** = Osmotic pressure. Q = Permeability.

Therefore this equation strictly says that the membrane is permeable to water, but it is impermeable to osmotic agents.

Rate of Drug Delivery from the Device Is Directly Proportional To The:

- Amount of osmotic agents in the device.
- Drug solubility modifier ratio.
- Level of pore former.
- Thickness and composition of semi permeable membranes.
- Size of hole/ aperture.
- Surface area of the device.

The Drug Release Is Inversely Proportional To: Concentration of polymer coating. Membrane thickness or weight gain.

Principle Components of Osmotic Drug Delivery System: (1) Drug, (2) Semipermeable membrane, (3) Osmotic agent (or) Osmogen, (4) Pore-forming agent, (5) Wicking agent, (6) Coating solvents, (7) Flux Regulators, (8) Plasticisers, (9) Solubilizing agents, (10) Surfactants.

Drug [13, 27]: All drugs are not suitable to develop as an osmotic drug delivery device. Examples of some drugs that are suitable to develop into osmotic drug delivery are given in **Table 2.** Basic characteristics that are required for a drug to develop into osmotic drug delivery system are as follows. Should have a short biological half-life 2-6 h. It should be a highly potent drug. Solubility should not be either high or low. Drugs should be suitable for prolonged treatment. The drug should itself have an osmogenicproperty and should have a good aqueous solubility. If the drug should not possess osmotic properties, then osmotic salts and other sugars are incorporated in the formulation.

Semi-Permeable Membrane [28, 52]: The membrane which is present in the osmotic drug delivery system is semipermeable in nature. So, the polymers that are used in this system should be permeable to water and impermeable to solutes that

are present. The semipermeable membrane plays an important role in the osmotic drug delivery system, so we have to be very careful in the selection of material for the semipermeable membrane.

The semipermeable membrane must meet some criteria, they are. It should be permeable to water. It should have sufficient wetting strength and wet modulus in order to retain its shape during the lifetime of the device. The Leakiness and reflection coefficient of an osmotic agent should approach the limiting value. Membrane should be biocompatible.

Osmotic Agent (or) Osmogen [25, 33, 35]: Osmotic agents (or) Osmogen are the essential ingredients in the osmotic drug delivery formulation. These osmogents are the materials that are used to create osmotic pressure inside the system. Osmotic agents or osmogens protect the concentration gradient across the membrane. They also create a driving force for the uptake of water and helps in and also helps in maintaining drug consistency in the hydrated form. Upon the perception of biological fluid into the osmotic device through a semipermeable membrane, then the osmogents are dissolved in the penetrated fluids, so that the osmotic pressure is created, inside the pump where due to high osmotic pressure the drug or medicament which is present inside the device and pushes the medicament outside through delivery orifice, in a controlled manner.

The release rate from the device is purely based on the osmotic pressure that is created inside the device. So in order to maintain the drug release rate osmotic agents are added to the formulation. When the drug solubility is low, then it shows a zero-order release. The most commonly used osmogents are given in **Table 2.** Osmotic agents used in the formulation either alone or in combination (mixture) of osmogents. Different types of osmogents present are (1) Water-soluble salts of inorganic acids, (2) -soluble salts of organic acids, (3) Carbohydrates, (4) Water-soluble amino acids and organic polymeric Osmogens.

Pore Forming Agents (Or) Channellingagents [36, 41]: Pore-forming agents are the materials that are used for the formation of microporous membranes. The microporous wall may be formed *in-vivo* by the former pore agent by its percolation of fluids during the operation of the system. These pore-forming agents are particularly used in the development of poorly water-soluble drugs and used in the preparation of multi particulate and controlled porosity osmotic pumps. The pore-forming agents may be organic or inorganic and also either in solid or in liquid form. Different examples of pore-forming agents are given in **Table 2.** These pore-forming agents are also called channelling agents. When the dissolution fluid comes in contact with the semipermeable membrane, then due to the presence of pore formers or channelling agent forms a pore on the semipermeable membrane, through which the drug releases in a controlled manner.

Wicking Agents [32, 42]: Wicking agent is defined as the material that has the ability to pull up water into a porous network of the drug delivery device. Also, these wicking agents have the ability to increase the contact surface area of the drug with the incoming aqueous fluid. These agents are either swellable or Non-swellable in nature; different examples of wicking agents are mentioned in **Table 2.** And these are characterized by having an ability to undergo physisorption with water. The main function of this wicking agent is to carry water to the surface inside the tablet core by creating a channel. The use of these wicking agents in the drug delivery device is to enhance the drug release from the orifice of the device.

Coating Solvents [44, 46]: Solvents that are suitable for making a polymeric solution is used in the preparation of coating material. The main function of these solvents is to disperse the polymer and other additives that are used for coating an osmotic device. Inert inorganic and organic solvents are used in the preparation of the outer layer or walls of osmotic drug delivery devices. Examples of different types of solvents are given in **Table 2.**

Flux Regulators [47, 48]: In order to regulate the flow of fluids into the drug delivery device, flux regulators are incorporated in the layer of the drug device, *i.e.* these flux regulators are added to the wall forming agents. There are different types of flux regulators used are hydrophilic and hydrophobic substances. Examples of flux regulators are given in **Table 2.**

Plasticizers [47, 51]: Plasticizers have the capacity to change the visco-elastic nature of the polymer, so these plasticizers are used in the coating membrane of the osmotic drug delivery systems.

Due to the addition of these plasticizers, the permeability of film may change. Plasticizers have the capacity to turn a hard and brittle polymer into a softer, more pliable material and possibly make the upper layer or film more resistant to mechanical stress. Different types of plasticizers are given in **Table 2.**

Solubilizing Agents [52]: Solubilizing agents are used to increasing the solubility of drugs in the gastrointestinal tract. Primarily used in the osmotic systems that contain low soluble drugs. Examples of these solubilizing agents are given in **Table 2.**

Surfactants [53]: Surfactants are the agents that act by modifying the surface energy of resources to get better their blending into the compound and upload their reliability in the environment of use during the drug release period. Some examples of surfactants are given in **Table 2.**

TABLE 2: TABLE SHOWING DIFFERENT EXAMPLES OF THE PRINCIPLE COMPONENTS USED IN THE OSMOTIC DRUG DELIVERY SYSTEM

Drugs [13–17]	**Semipermeable membrane [28–32]**	**Pore-forming agents [36–41]**
Prazosin	Cellulose acetate	Alkaline metal salts
Phenylpropanolamine	Ethylcellulose	Potassium sulphate, Potassium
Doxazosin	Cellulose acetate butyrate	phosphate, Sodium chloride, Sodium
Verapamil	Cellulose propionate	bromide, Potassium chloride *etc*
Oxybutynin chloride	Cellulose acetate	Alkaline earth metals
Isradipine	Cellulose diacetate	Calcium chloride, calcium nitrate
Paliperidone	Cellulose triacetate	Carbohydrates
Chlorpheniramine maleate	Agar acetate	Sucrose, Glucose, Fructose, Mannose
Glipizide	Amylose triacetate	Lactose, Sorbitol, Mannitol
Nifedipine	Beta-glucan acetate	Volatile pore formers
Pseudoephedrine	Poly(vinyl methyl) ether copolymers	Ethanol and Butanol
Salbutamol	Poly (orthoesters)	Non-volatile pore formers
Carbamazepine	Polyacetals	Glycerol and Water
Leuprolide acetate	Poly(glycolic acid)	Diols and Polyols
Sufentanil	Poly(lactic acid) derivatives	Polyhydric alcohol, Dibutyl phthalate
Methylphenidate	Eudragits	Polyvinyl pyrrolidone
Albuterol		

Examples of Osmotic Agents used in Osmotic Drug Delivery. [25 33–36]	
Examples of osmotic agents [25]	**Some mixtures used as osmotic agents [33–36]**
Carbohydrates	(1) Mannitol +Sucrose 170
Maltose, Lactose, Mannose, sucrose	(2) Dextrose +Sucrose 190
Water-soluble amino acids and organic polymeric Osmogens	(3) Mannitol +Dextrose 225
Polyvinyl pyrrolidone, Polyethylene oxide	(4) Mannitol +Fructose 415
Methylcellulose, Hydroxyethyl methylcellulose	(5) Lactose +Dextrose 225
Hydroxypropyl methylcellulose, Sodium carboxymethyl cellulose	(6) Lactose +Fructose 500
Water-soluble salts of inorganic acids	(7) Dextrose +Fructose 450
Sodium or potassium hydrogen phosphate, Sodium, or Potassium chloride	(8) Sucrose-fructose 430
Magnesium chloride or sulfate, Lithium, Sodium phosphate dibasic. 7 H_2O, Sodium	(9) Lactose- sucrose 250
phosphate tribasic. 12 H_2O, Sodium phosphate dibasic. 12 H_2O, Sodium phosphate	(10) Mannitol - lactose 190
monobasic. H_2O, Sodium phosphate dibasic. Anhydrous	
Water-soluble salts of organic acids	
Magnesium succinate, Sodium benzoate, Sodium and potassium acetate, Sodium	
citrate, Sodium ascorbate, Potassium sulphate	

Wicking agents [32–42]	**Coating solvents [44–46]**	**Mixture of solvents :**
(M-pyrol,		
Bentonite,	Typical solvents used :	Acetone-Methanol (80:20)
Aluminium silicate,	Ethyl acetate,	Chloride-Methanol-Water (75:22:3)
Polyester,	Cyclohexane,	Acetone-Ethanol (80:20)
Polyethylene,	Carbon tetrachloride,	Acetone-Water (90:10)
Colloidal silicon dioxide,	Water,	Methylene chloride - methanol (79:21)
Kaolin,	Methylene chloride,	
Titanium dioxide,	Acetone,	

Alumina (10) Niacinamide (11) Sodium lauryl sulphate (SLS) (12)Low molecular weight poly vinyl pyrrolidone (PVP)	Methanol (8) Ethanol (9) Isopropyl alcohol (10) Butyl alcohol	
Flux regulators [47–48]	**Plasticizers [47–51]**	**Surfactants [53]**
Hydrophilic substances Polyethethylene glycols (300 to 6000 Da), Polyhydric alcohols Polyalkylene glycols Hydrophobic substances Phthalates substituted with an alkyl or alkoxy (e.g., Diethyl phthalate or Di methoxy ethyl phthalate)	PEG-600 PEG-200 Triacetin (TA) Dibutyl sebacate Ethylene glycol monoacetate Ethylene glycol diacetate Triethyl phosphate, and diethyl tartrate	Polyoxyethylene glyceryl ricinoleate Polyoxyethylated castor oil having ethylene oxide Glyceryl laureates Glycerol (sorbitan oleate, stearate or laurate)
Solubilizing agents [52]		
(1) Agents that inhibit crystal formation of drugs Polyvinyl pyrrolidone (PVP), poly (ethylene glycol) (PEG 8000) and βcyclodextrin) (2) Micelle-forming agents with a high HLB value Tween 20, 60, and 80, polyoxyethylene or polyethylene containing surfactants and other long-chain anionic surfactants such as Sodium Lauryl Sulfate) (3) Citrate esters Alkyl esters especially triethyl citrate (4) Combinations of complexing agents Polyvinyl pyrrolidone (PVP) and poly(ethylene glycol) with anionic surfactants such as SLS are mostly preferred		

Types of Osmotic Drug Delivery System [10, 27]: There are two different types of osmotically controlled drug delivery system. They are as follows in **Table 3**.

Implantable osmotic drug delivery system	**Oral osmotic drug delivery system**
Rose Nelson pump.	Elementary osmotic pump.
Higuchi leeper osmotic pump.	Push-pull osmotic pumps.
Higuchi theeuwes osmotic pump.	Sandwiched osmotic pump.
Alzet osmotic pump.	Osmotic pump with non expanding second chamber.
DUROS® osmotic pump.	Asymmetric membrane osmotic pump.
Implantable mini osmotic pump.	Liquid osmotic system (L-OROS).
	L-OROS soft gelatin capsule.
	Controlled-porosity osmotic pumps.
	Osmotic bursting osmotic pump
	Monolithic osmotic pump tablet.
	OROS-CT (colon targeting).
	Effervescent Osmotic pump Tablet.
	Multiparticulate Delayed-Release System.
	Self Emulsified Osmotic Tablet.

TABLE 3: TYPES OF IMPLANTABLE OSMOTIC DRUG DELIVERY SYSTEM

Pump Type	Description
Rose Nelson pump. [54–55]	The earliest discovery of all osmotic pumps is the Rose Nelson pump. It mainly consists of three chambers, namely Drug, Salt, and water chamber. Where it contains a semipermeable membrane between the salt and water chamber and an elastic diaphragm between the drug and salt chamber. As the concentration of water is low, the water moves into the salt chamber through the semipermeable membrane via the osmosis process. Due to the water movement into the salt chamber, the pressure inside the salt chamber increases. The elastic diaphragm, which is present b/w the salt and drug chamber, pushes towards the drug chamber; this drug pushes out from the chamber through delivery orifice. The pictorial representation of the Rose nelson pump was shown in Fig :- 2. Note:- The major limitation of this Rose nelson pump is the water chamber needs charging before it can be used. Mainly used for the drugs to treat sheep and cattle gut.
Higuchi leeper osmotic pump.[56–59]	This pump doesn't have any water chamber in it, but it contains a porous membrane along with a semipermeable membrane. The water enters into the device through the semipermeable with the help of a porous membrane. The salt chamber in the device contains a saturated solution. After the implantation of

	the device into the body the biological fluids enter into the device so that the salt which is present in the device dissolves and osmotic pressure is created in the device; due to this, the movable separator moves toward the drug chamber in order to exclude the drug outside the device. The pictorial representation of the Higuchi Leeper pump was shown in Fig:- 3. This osmotic pump is widely used for veterinary purposes to deliver antibiotics or growth hormones to animals. Due to the absence of an inbuilt water chamber, this device is less susceptible to microbial contamination.
Higuchi theeuwes osmotic pump.[60–63]	Almost similar to the Higuchi-Leeper pump and it was a simplified version of the Rose-nelson pump. This higuchitheeuwes osmotic pump contains a semipermeable membrane attached to the outer rigid housing of the device. Beneath the outermost layer there is a solid osmogen, dispersed in a suitable solvent, and the innermost layers of the device consist of flexible and collapsible material. And the drug reservoir is in direct contact with the delivery orifice. The pictorial representation of Higuchi the ewes osmotic pump was shown in Fig :- 4. When this Higuchitheeuwes osmotic pump comes in contact with the body fluid, the water enters inside the pump through the semipermeable membrane so that the osmotic pressure was developed inside the device pressure exerts on the innermost flexible walls so that due to the increased pressure the drug delivers outside. Most of these pumps use the dispersion of solid salt in a suitable carrier for the salt chamber of the device.
Alzet osmotic pump [64]	It is an osmotic pump in which the core of the device is filled with the drug or hormone solution which is to be delivered, and the salt chamber surrounds it with the impermeable layer between them. The pictorial representation of this Alzet osmotic pump was shown in Fig:- 5. When this alzet osmotic pump comes in contact with the water, the water enters into the salt chamber through a semipermeable membrane. The osmotic pressure inside the osmotic pump increases and causes the compression of a flexible reservoir, due to which the drug solution comes out. It is the most widely used osmotic pump for laboratory animals. This pump is used to deliver homogenous solutions or suspensions continuously at a controlled rate for an extended period of time (usually 14 days).
DUROS® osmotic pump. [65]	Duro's osmotic pump is a small rod-shaped implantable osmotic device with titanium housing. Where it consists of a semipermeable membrane, next to this, it contains an osmotic engine and piston, and next to this, the drug reservoir is present. The pictorial representation of this Duro's osmotic pump was shown in Fig:- 6 When this pump comes in contact with the water, then the water is slowly drawn into the pump through the semipermeable membrane by the osmotic agent residing in the engine compartment, thereby the osmotic agent expands and exerts a pressure on the piston due to this the piston moves forward there by the drug releases out from the device. Mostly used for systemic and site-specific administration and has the benefit of providing continuous therapy for up to one year. The non-biodegradable, osmotically driven system is intended to enable the delivery of small drugs, peptides, proteins, DNA, and other bioactive macromolecules for systemic or tissue-specific therapy. The first marketed product to incorporate DUROS®, is indicated for the palliative treatment of advanced prostate cancer.
Implantable mini osmotic pump [56]	This pump is almost similar to the Higuchi-Theeuwes pump, but it has an additional component *i.e,* a flow modulator that is inserted inside while the device is already filled with the drug solution or suspension. These implantable mini osmotic pumps are available with various delivery rates in the range between 0.25 to 10ml per hour and delivery duration between one day and four weeks and release the drug at a controlled rate for an extended period of time. The implantable mini osmotic pump was shown in Fig:- 7

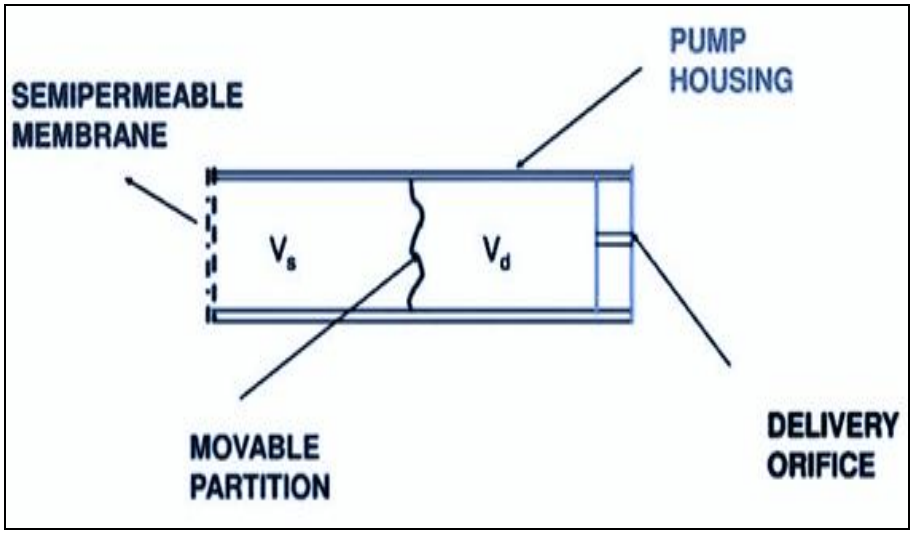


FIG. 1: SHOWING THE SCHEMATIC REPRESENTATION OF THE BASIC MODEL OF OSMOTIC PRESSURE POWERED DRUG DELIVERY SYSTEMS

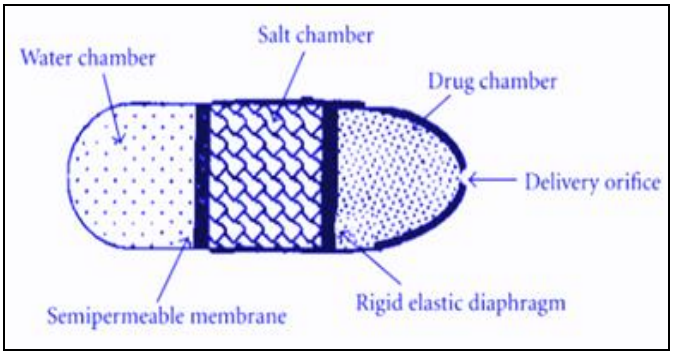


FIG. 2: ROSE NELSON PUMP

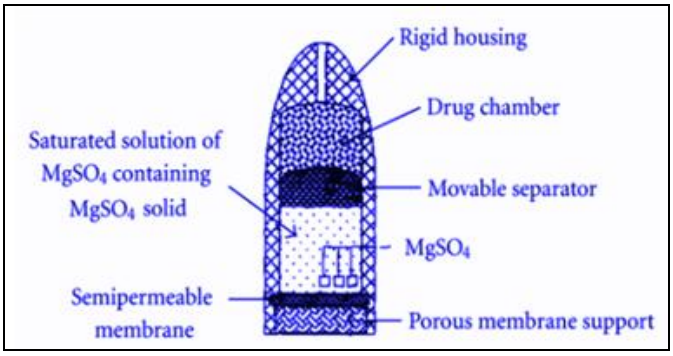


FIG. 3: HIGUCHI LEEPER OSMOTIC PUMP

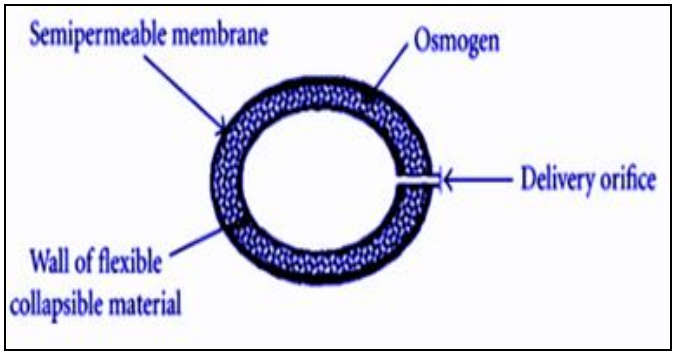


FIG. 4: HIGUCHI THEEUWES OSMOTIC PUMP

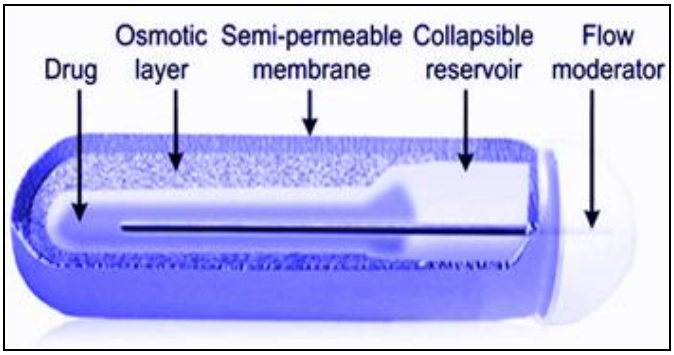
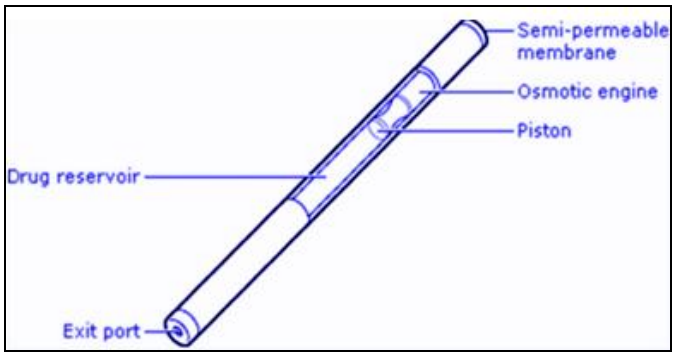


FIG. 5: ALZET OSMOTIC PUMP



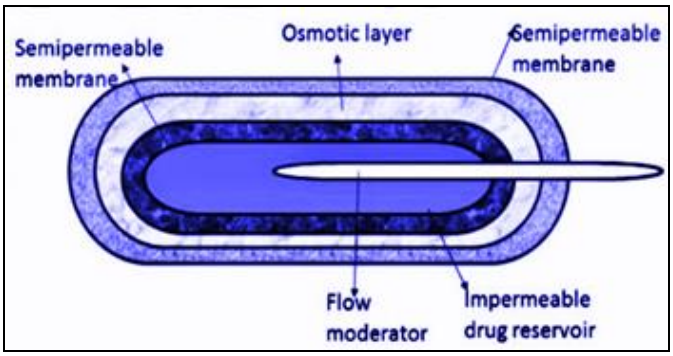


FIG. 6: DUROS OSMOTIC PUMP. FIG. 7: IMPLANTABLE MINI OSMOTIC PUMP

TYPES OF ORAL OSMOTIC DRUG DELIVERY SYSTEM

Pump Type	Description
Elementary osmotic pump [68–69]	It consists of an osmotic core containing the drug, which is surrounded by a rate-controlling semipermeable membrane and also contains a laser-drilled delivery orifice. The delivery orifice size is most critical in the semi permeable membrane through which the active agent i.e the drug is delivered. The pictorial representation of the elementary osmotic pump is shown in Fig :- 8. Then this osmotic device comes in contact with fluids; these fluids enter into the device so that the saturated solution of the drug in the core is formed inside the osmotic pump. Then this saturated drug solution is dispensed out from the delivery device at a controlled rate. Elementary osmotic pumps release drugs at a zero-order release rate for a prolonged period of time, at a controlled rate. The main disadvantage of the elementary osmotic pump is that it is only suitable for the delivery of water-soluble drugs.
Push-pull osmotic pump [70–72]	It is a modified form of an elementary osmotic pump. Push-pull osmotic pump contains two layers the upper layer and lower layer where the upper layer contains the drug in a formulation with an osmotic agent and the lower layer contains polymeric osmogents with excipients which in turn coated with the semipermeable membrane (It regulates water influx into both layers) and a drug delivery orifice. The pictorial representation of the push-pull osmotic pump is shown in Fig :- 9. When this push-pull osmotic pump comes in contact with the aqueous fluid, the fluid enters the system; thereby, the polymeric osmotic layer swells and pushes the drug layer; due to this, the drug releases from the osmotic pump through a delivery orifice. The main advantage of this push-pull osmotic pump is, it is suitable for both poorly water-soluble drugs and highly water-soluble drugs. In push-pull osmotic pumps, the pressure is enough in order to release the drug under zero-order kinetics.

Sandwiched osmotic pump [73]	Sandwiched osmotic pump composed of a polymeric push layer which is sandwiched between two drug layers with the two delivery orifices. The pictorial representation of the sandwiched osmotic pump is shown in the Fig :- 10. When this sandwiched osmotic system comes in contact with water then the water enters the system and the middle push layer which contains a swelling agent swells so that the push layer pushes the both drug layer due to this the drug releases from orifices on both sides. Main advantage of this system is the drug present in both the layers and also we can prepare this with two different drugs.It can be used for drugs to cause local irritation of gastric mucosa.
Osmotic pump with non-expanding second chamber [74–75]	It contains a non-expandable second chamber, in this device there are two rigid chambers, whereas the first chamber contains a biologically inert osmotic agent, such as sugar or a simple salt like sodium chloride, and in the second chamber contains a drug. The pictorial representation of an osmotic pump with non-expanding second chamber is shown in theFig :- 11.When this device comes in contact with water then the water is drawn into both the chambers with the help of semi permeable membranes. Due to this the osmotic agent solution was formed in the first chamber, then passes through the connecting hole to the drug chamber where it mixes with the drug solution and due to this pressure increases and drug releases out from the device. This device is used to deliver relatively insoluble drugs.
Asymmetric membrane osmotic pump [76–77]	It contains a capsule wall with insoluble water semipermeable polymeric membrane. The pictorial representation of an Asymmetric membrane osmotic pump was shown in the Fig :- 12. Imbibition of water into the asymmetric membrane osmotic pump through the semipermeable membrane. Due to this, the components inside the device solubilizes. Therefore, pressure inside the device increases, and the solution releases out from the same polymeric membrane. The main advantage of this system is high water permeability, and there is no pore formation (on porosity).
Liquid osmotic system (Hard L-OROS) [78]	L-OROS hard cap is one type of liquid osmotic system. This system consists of a hard gelatin capsule containing a liquid gelatin capsule, a barrier layer, and a push layer surrounded by a semipermeable membrane. The pictorial representation of L-OROS hard cap was shown in theFig :- 13. The L-OROS hard cap hard cap system was specially designed to accommodate more viscous suspensions with higher drug loading capacity than would be possible using soft gelatin capsules. The expansion of the barrier layer inside the hard gelatin capsule results in the development of hydrostatic pressure inside the system, thereby forcing the liquid suspension formulation to break through the hydrated gelatin capsule shell at the delivery orifice. When this device comes in contact with water, this water imbibes across the Semipermeable membrane, expanding the osmotic engine, pushing against the barrier and releasing the drug through the delivery orifice. Mainly suitable for the delivery of lipophilic drugs.
L-OROS soft gelatin capsule [78–80]	L-OROS soft cap contains a drug formulation in a soft gelatin capsule surrounded by a barrier layer, osmotic layer, a Semipermeable membrane, and a delivery orifice. The delivery orifice is designed through these three layers. The pictorial representation of L-OROS soft gelatin capsule was shown in Fig :- 14. When this L-OROS soft gelatin capsule comes in contact with the water, then the water imbibes across the Semipermeable membrane; due to this hydrostatic pressure was developed inside the device, so that the liquid formulation comes out from the hydrated gelatin capsule through the delivery orifice. It is well-suited for the delivery of insoluble drugs and macromolecules such as polysaccharides and polypeptides. The main advantage of this system is that it provides a continuous delivery of liquid suspension drug formulation and improves drugs' bioavailability.
Telescopic Capsule for Delayed-Release [80–84]	It contains a dispenser that comprises a housing with a first wall and second wall sections in a slidable telescopic arrangement. This housing maintains integrity in its environment of use. This device mainly consists of two chambers, where the first chamber contains the drug and a delivery port. The second chamber contains an osmotic engine. A small layer of wax-like material separates the two chambers. And the desired active agent is placed into one of the chambers by using manual or automated filing mechanisms.. The open end of the filled vessel is fitted in the open end of the cap, and the two pieces are compressed together until the cap, osmotic bilayer tablet, and vessel fit together tightly. The pictorial representation of a telescopic capsule for delayed release was shown in fig :- 15. As fluid is entered into the housing of the dispensing device, the osmotic engine expands, due to this it exerts pressure on the slidable connected first and second wall chambers. During the delay period, the reservoir volume containing the active ingredient was kept constant, and therefore, a negligible pressure existed between the environment and the interior of the reservoir. As a result of this the flow of environmental fluid by the pressure that enters into the reservoir is minimum so that no agent is delivered for a period of time.
Controlled- porosity osmotic pumps [90–91]	Controlled porosity osmotic pump consists of a core with the drug surrounded by a semipermeable membrane, and this membrane contains different channeling agents of water-soluble additives in the coating. And these additives when they comes in contact with water they dissolve which results in an in-situ formation of a microporous membrane. So that the resulting microporous membrane is permeable to both water and dissolved solutes. And the mechanism of drug release from this system

	was found to be primarily osmotic and then simple diffusion. The pictorial representation of controlled porosity osmotic pump was shown in Fig 16. The main advantage of this system is stomach irritation problems can be considerably reduced because the drug is released from the whole of the device surface rather than from a single hole.
Osmotic Bursting osmotic pumps [88–89]	This osmotic bursting osmotic pump is similar to elementary osmotic pumps but this does not contain a delivery orifice. It consists of a solid core that has a film coat. The pictorial representation of Osmotic Bursting osmotic pumps was shown in Fig 17. When it comes in contact with water, this water enters the system as a result of this osmotic pressure is developed inside the system due to this the outer film ruptures and the inner contents released outside. This system is used to provide pulsatile release. In this the release rate can be controlled by increasing the thickness of the oute coated film.
Monolith osmotic pump tablet [85–89]	It consists of a simple dispersion of a water soluble agent in a polymeric matrix. The pictorial representation of the Monolith osmotic pump tablet was shown in Fig 18. When it comes in contact with water, then the water enters into the system by the vigorous agent that ruptures the polymer matrix capsule surrounding the agent, thus healing the drug to the outside environment. If more than 20-30 volumes per liter of the active agents is incorporated into the device then the usage of this system is not possible.
OROS-CT (Colon targeting) [90–94]	This is the system that contains a single or as many as five to six push-pull osmotic pumping agents, where these are filled as a unit in a hard gelatin capsule. Also it consists of a semipermeable membrane surrounded by an enteric coat and a core. The pictorial representation of OROS-CT (Colon targeting) was shown in Fig 19. When this system comes in contact with gastric fluids, due to this the gelatin capsule was dissolved, and the enteric coating which is present on the osmotic pumps prevents the entry of fluids from the stomach to the system where this prevents the degradation of drug in the stomach pH
Self Emulsified osmotic system [95]	Self Emulsified osmotic system contains a self-emulsifying agent. This system contains a slightly soluble or insoluble drugs and self-emulsifying agent in the table core. This emulsifying agent emulsifies the drug present inside the system. This Self emulsifying system improves the controlled release rate, bioavailability of drugs and makes the plasma concentrations more stable. The pictorial representation of Self Emulsified osmotic system was shown in Fig 20.
Multi layer osmotic system [96–97]	It contains two compartments, the upper compartment, usually, the drug compartment, contains the drug along with osmotically active agents and the Lower compartment usually the push compartment, contains the polymeric osmotic agents. The pictorial representation of the Multilayer osmotic system was shown in Fig :- 21. When this dosage form comes in contact with the water, both compartments absorb the water at the same time as the lower segment is lacking any orifice, then it expands and pushes the diaphragm into the higher drug chamber, thereby drug releases via the delivery orifice.
Floating Elementary osmotic pump tablet [66–67]	This floating elementary osmotic pump can flow within the stomach. Inside this system, there is an Elementary osmotic pump tablet surrounded by the gas generating layer (Gas generating agent + Gelling agent). This gas generates a layer inturn surrounded by a polymeric film layer and an orifice. The pictorial representation of this floating elementary osmotic pump was shown in Fig 22. When this tablet comes in contact with the solvents like water or gastric fluids, these solvents enter into the tablet to produce the gas in the gas generating layer. Then the produced CO_2 gas bubbles were entrapped by the gelling agent in the gas generating layer. Thereby the system floats and results in drug release, as shown in Fig 22.

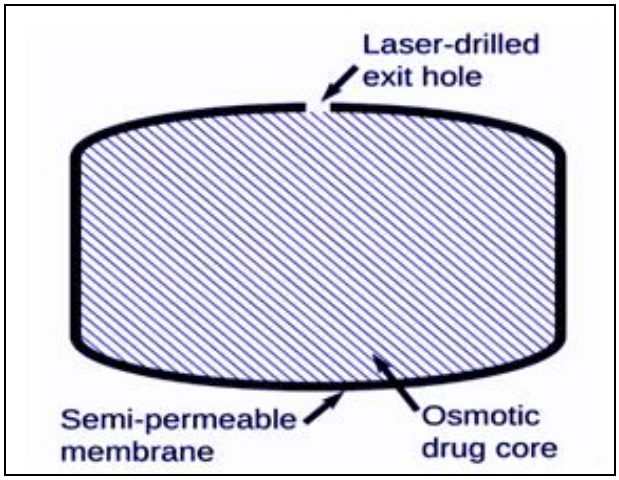


FIG. 8: ELEMENTARY OSMOTIC PUMP

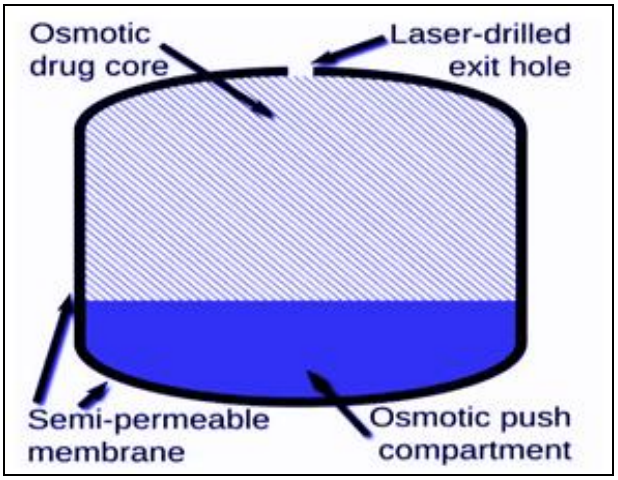


FIG. 9: PUSH-PULL OSMOTIC PUMP

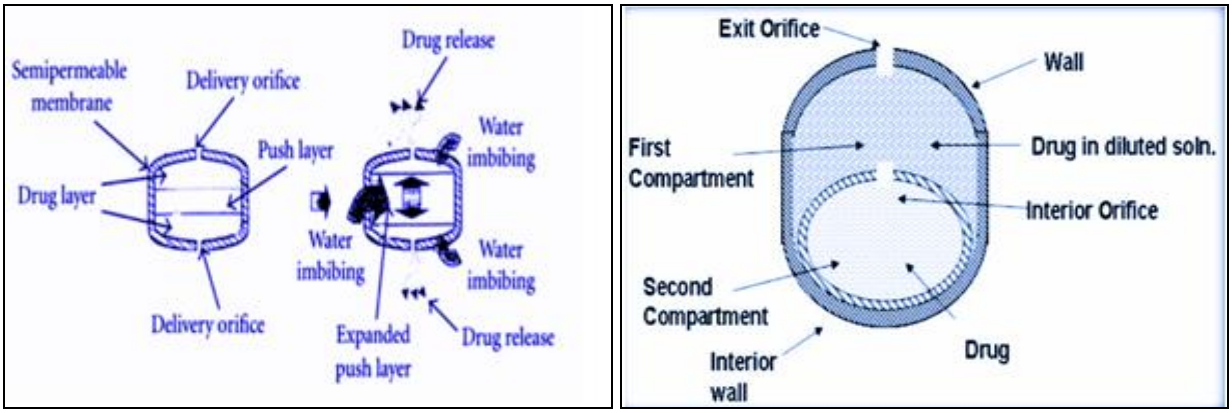


FIG. 10, 11: SANDWICHED OSMOTIC PUMP, OSMOTIC PUMP WITH NON EXPANDING SECOND CHAMBER

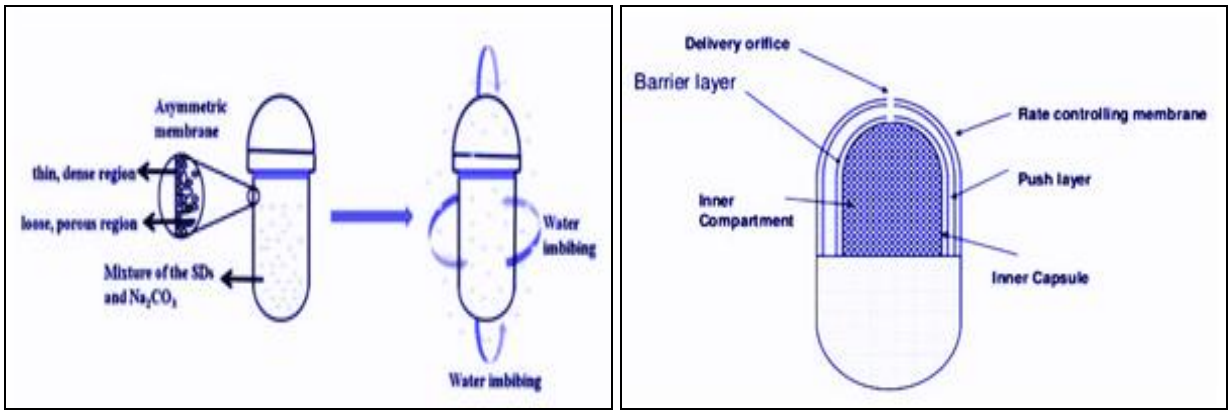


FIG. 12, 13: ASYMMETRIC MEMBRANE OSMOTIC PUMP, LIQUID OSMOTIC SYSTEM (L-OROS)

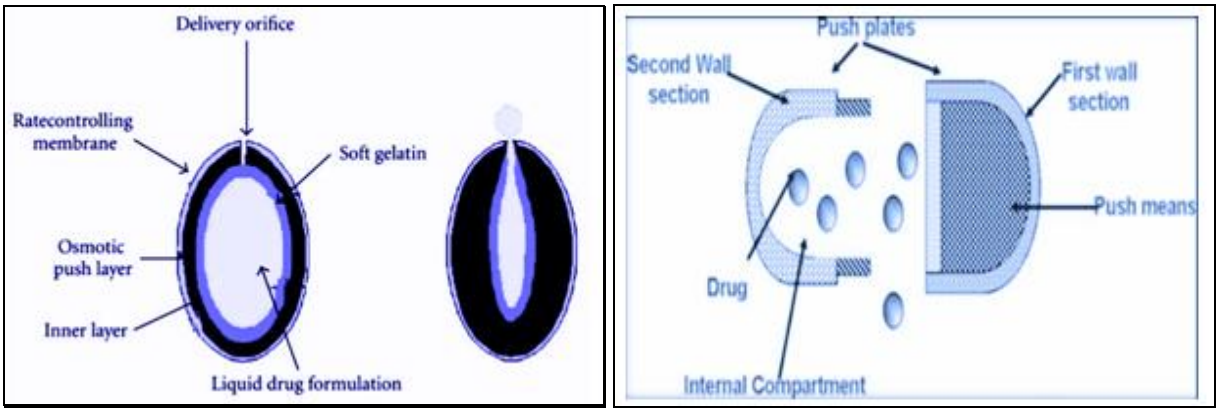


FIG. 14, 15: L-OROS SOFT GELATIN CAPSULE, TELESCOPIC CAPSULE FOR DELAYED RELEASE

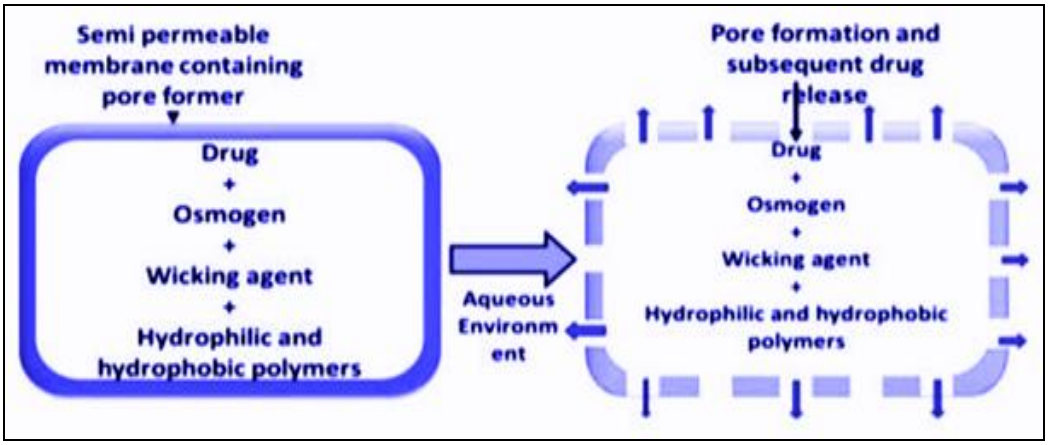


FIG. 16: CONTROLLED-POROSITY OSMOTIC PUMPS

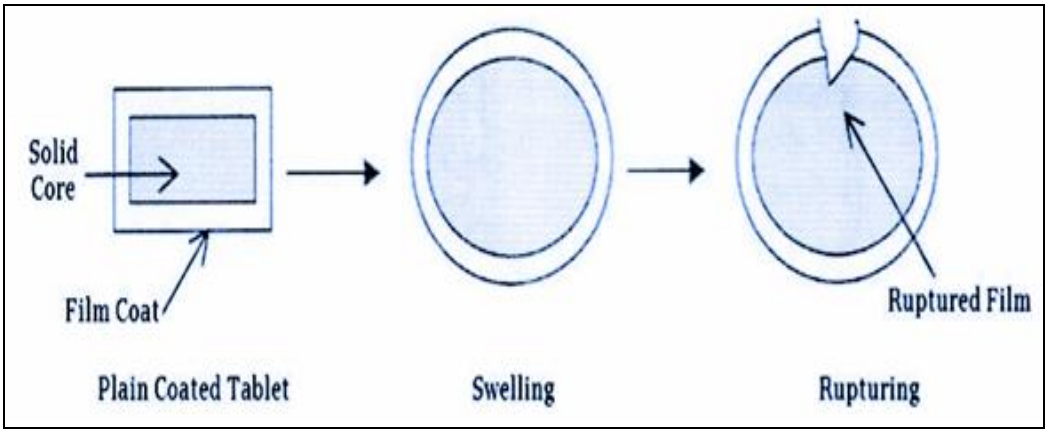


FIG. 17: OSMOTIC BURSTING OSMOTIC PUMPS

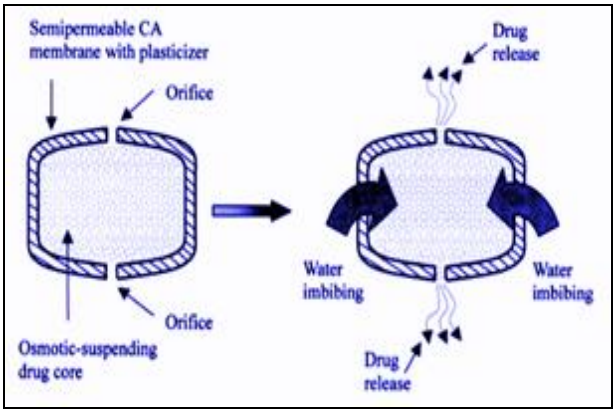


FIG. 18: MONOLITHIC OSMOTIC PUMP TABLET

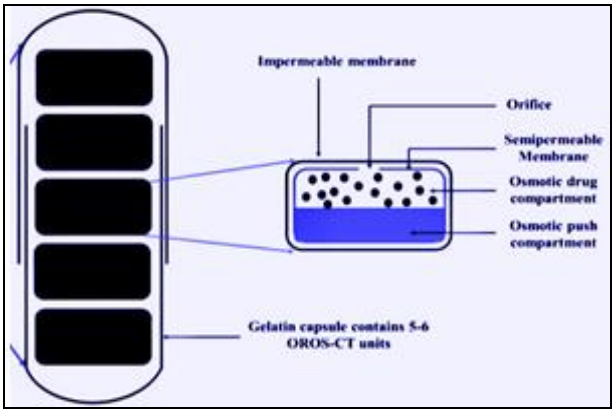
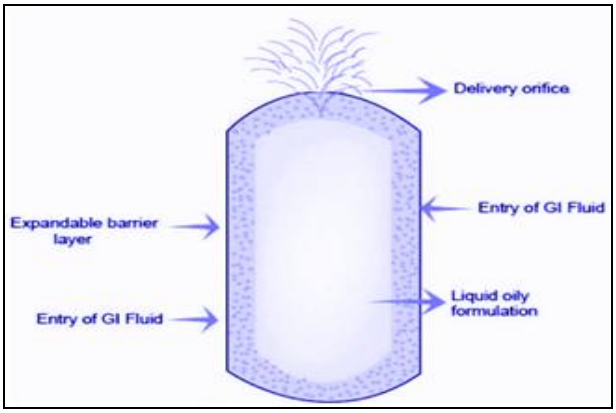


FIG. 19: OROS-CT COLON TARGETING



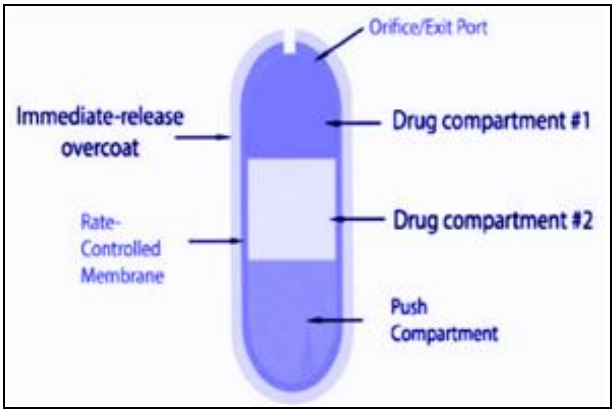


FIG. 20, 21: SELF EMULSIFIED OSMOTIC SYSTEM MULTI, PARTICULATE DELAYED RELEASE SYSTEM

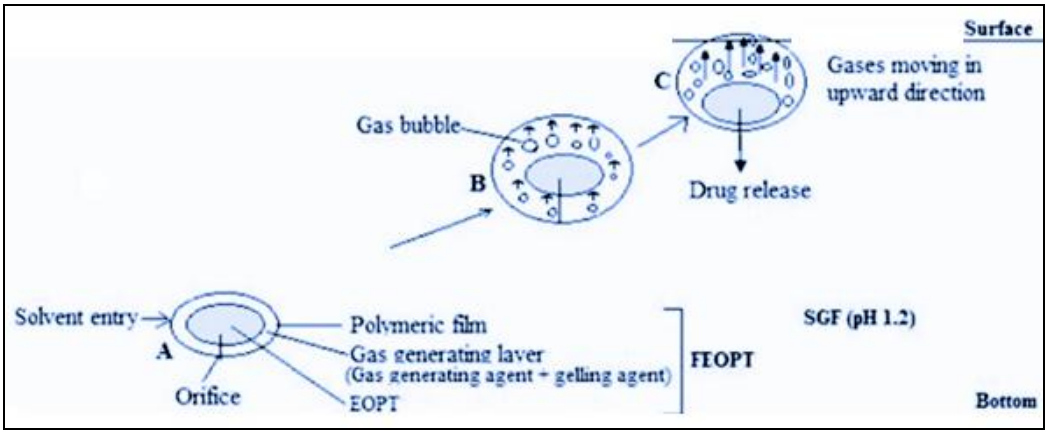
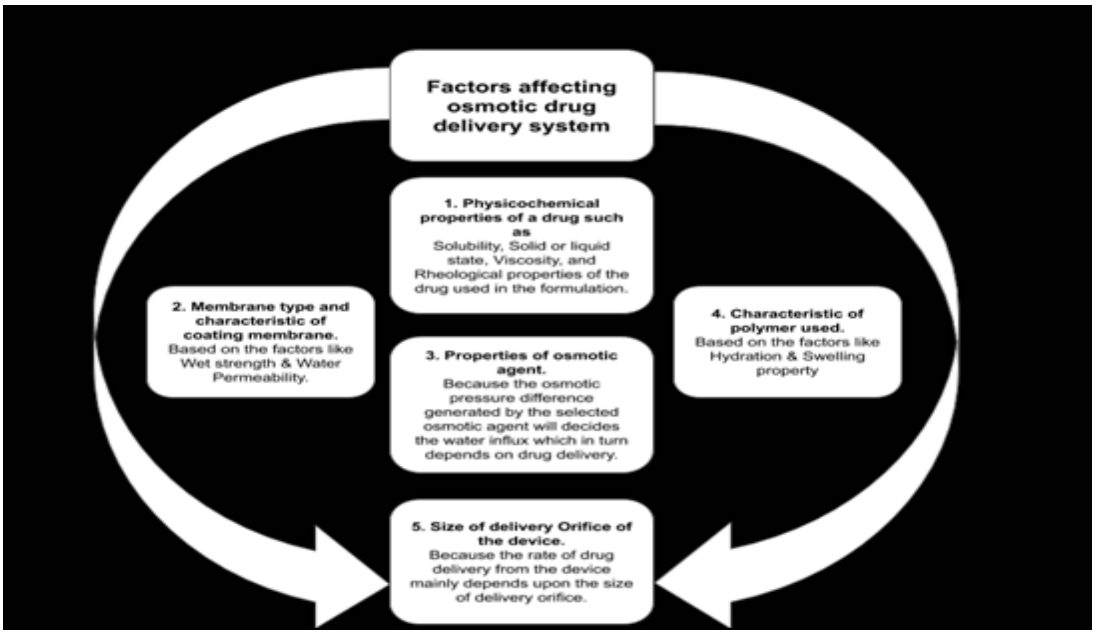


FIG. 22: FLOATING ELEMENTARY OSMOTIC PUMP TABLET

Creation of Delivery Orifice [103, 104]: Delivery orifice for the osmotic drug delivery devices may be created by using different mechanical drilling equipment, Some of the methods to produce a delivery orifice in the osmotic tablet coating are (1) Laser Drill, (2) Indentation that is Not Covered During the Coating Process, (3) Use of Leachable Substances in the Semi-Permeable Coating, (4). Systems with Passageway Produced In-Situ are some of the methods to make a delivery orifice. Out of which laser drilling technique is a mostly used technique for the creation of delivery orifice to the osmotic tablet, the main mechanism involved in this technique is the laser beam is projected on the surface of the tablet then it absorbs the energy of the beam and gets heated that causing a hole to the tablet wall which is a delivery orifice. And the size of the delivery orifice can be controlled by varying different parameters like by controlling the laser power, firing duration (pulse time), the thickness of the wall, and the dimensions of the beam at the wall. Whereas in some osmotic drug delivery systems we can see the in situ formation of delivery orifice that is achieved by incorporating different types of pore-forming agents (these pore-forming agents are water-soluble) in the wall during the coating process. The size of the delivery orifice must be perfect for controlling the drug release from the osmotic device. And the size of the delivery orifice should not also be too large or too small because if it is too large, the drug solute diffusion from the orifice may take place. Or if the size of the delivery orifice is too small, then it will affect the zero-order delivery due to the development of hydrostatic pressure within the core. So the delivery orifice size must be appropriate to achieve the desired drug release from the osmotic device. And the size of the delivery orifice should not also be too large or too small because if it is too large, the drug solute diffusion from the orifice may take place. Or if the size of the delivery orifice is too small, then it will affect the zero-order delivery due to the development of hydrostatic pressure within the core. So the delivery orifice size must be appropriate to achieve the desired drug release from the osmotic device.

Factors Affecting Osmotic Drug Delivery System [98, 104]:



Evaluation Parameters [105, 106]: Evaluation of osmotic drug delivery devices can be done by studying the following parameters, Hardness, Weight Variation, Visual Inspection Of Tablets, Coating Thickness & Coat Weight, Coating Uniformity, Friability, Pore (Or) Orifice Diameter, *In-vitro* Dissolution Studies, By Using Methods Like Vertically Reciprocating Shaker, Conventional Usp Dissolution Apparatus I And Ii, Flow-Through Apparatus, *In-vivo* Evaluation, *In-vitro* - In-vivo Correlation, Kinetics Of Drug Release.

SCIENTIFIC STUDIES [48, 56, 72, 95, 107, 112]

S. no.	Scientists	Studied On
1	Vincent Malaterre *et.al*	Studied on the release mechanism underlying the drug delivery from push-pull osmotic pumps (PPOP)
2	Wright *et.al*	Studied an osmotic controlled release bilayer tablet for water soluble drugs.
3	Herbig S. M. *et al*	He found a new type of asymmetric membrane tablet coatings offering significant advantages over conventional osmotic tablets
4	Toshiaki Nagakura *et al*	He designed an osmotic pump using a semipermeable membrane that changes its volume according to the concentration of the outside solution
5	Roger A. Rajewski *et al*	Studied the membrane controlling factors responsible for drug release from a controlled-porosity osmotic pump tablet (OPT) that utilizes sulfobutyl ether-- cyclodextrin, (SBE)7m --CD, both as solubilizing agent and osmotic agent
6	Hai Bang Lee *et al*	Studied the sandwiched osmotic tablet system (SOTS)
7	Sapna N *et al*	Developed a controlled porosity osmotic pump-based drug delivery system
8	Roger A. Rajewski *et al*	Investigated the application of controlled-porosity osmotic pump tablet (OPT) utilizing (SBE)7m --CD both as a solubilizer and an osmotic agent for drugs with varying physical properties
9	Pratim K Choudhury *et al*	Developed an asymmetric membrane capsule of cellulose acetate for osmotic delivery of flurbiprofen and influence of osmogents and solubilizing agent on in vitro drug release were evaluated
10	Longxiao Liu et al	Developed the bilayer-core osmotic pump tablet (OPT) for nifedipine which does not require laser drilling to form the drug delivery orifice
11	AK Philip *et al*	Developed an asymmetric membrane capsular system, formed in situ, for poorly water-soluble drug, ketoprofen
12	Mahalaxmi.R *et al*	Developed the extended-release controlled porosity osmotic pump formulations of model drug glipizide
13	Pramod Kumar *et al*	Developed an Elementary osmotic pump (EOP) of highly water-soluble drug tramadol hydrochloride (TRH)
14	WakodeRajeshri *et al*	Developed an oral monolithic osmotic system for highly water-soluble pramipexole dihydrochloride monohydrate
15	Mothilal M *et al*	Developed an osmotically controlled oral drug delivery system formulations of metoprolol succinate were prepared using different concentrations of mannitol by wet granulation technique

DIFFERENT MARKETED PRODUCTS

Trade Name	Design Type	Active Ingre Design Type Dient
Acutrim	Elementary osmotic pump	Phenylpropanolamine
Alpress LP	Push-Pull osmotic pump	Prazosin
Concerta	Implantable osmotic systems	ethylphenidatem
Chronogesic	Implantable osmotic systems	Sufentanil
Covera HS	Push-Pull with a time delay system	Verapamil
Calan SR	Push-Pull osmotic pump	Doxazosin
Calan SR	Push-Pull osmotic pump	Verapamil
Ditropan XL	Push-Pull osmotic pump	Oxybutynin chloride
Dynacirc CR	Push-Pull osmotic pump	Isradipine
Efidac 24	Elementary osmotic pump	Pseudoephedrine & Brompheniramine, Pseudoephedrine &
Sudafed 24	Elementary osmotic pump	Pseudoephedrine
Glucotrol XL	Push -Pull osmotic pump	Glipizide
Tegretol XR	Elementary osmotic pump	Carbamazepine
Viadur	Implantable osmotic systems	Leuprolide acetate
Volmax	Elementary osmotic pum Elementary osmotic pump p	Salbutamol
Minipress XL	Elementary osmotic pump	Prazosin
Procardia XL	Push-Pull osmotic pump	Nifedipine
Teczem	Push-Pull osmotic pump	Enalapril and Diltiazem
Adalat OROS	Oral Osmotic pump	Nifedipine
Ditropan XL/Lyrinel XL	Oral Osmotic pump	Oxybutynin
Exalgo/Jurnista	Oral Osmotic pump	Hydromorphone
Invega	Oral Osmotic pump	Palperidone
Efidac 24	Elementary osmotic pump	Chlorpheniramine maleate

CONCLUSION: In osmotic drug delivery systems, osmotic pressure plays an important role for the delivery of drugs from the device, due to the development of high osmotic pressure inside the osmotic system, the drug releases from the device. So it can be said that the drug release from the osmotic device is purely based on the osmotic pressure that is developed inside the system. In addition to these, there are many pulsatile-based delivery systems based on expandable orifice, lipid osmotic pumps, telescopic capsules containing mini osmotic pumps for delayed-release, osmotic bursting osmotic pump and many more osmotic systems are developed for controlled release. So It can be concluded that both implantable and oral osmotic drug delivery systems can be used in the field of controlled drug delivery systems. The development of these Osmotic drug delivery systems has gained a lot of importance with the appearance of new technologies and products.

ACKNOWLEDMENT: Nil

CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Prescott LF: The need for improved drug delivery in clinical practice, in: novel drug delivery and its therapeutic application, john wiley and sons. West Sussex UK 1989; 1-11.
2. Gupta, RN, Gupta R, Basniwal PK and Rathore GS: Osmotically controlled oral drug delivery systems: a review. International Journal of Pharmaceutical Sciences 2009; 1(2): 269-75.
3. RK Verma and S Garg: Current status of drug delivery technologies and future directions. Pharm Technol.-OnLine (http://www.pharmaportal.com) 2001; 25: 1-14.
4. Bhatt PP: Osmotic drug delivery systems for poorly water soluble drugs, Pharmaventures Ltd Oxford.
5. Ende MT, Herbig SM, Korsmeyer RW and Childlaw MB: Handbook of pharmaceutical controlled release technology. Marcel Dekker Inc New York 2005; 751.
6. F Theeuwes, DR Swanson, G Guittard, A Ayer and S Khanna: Osmotic delivery systems for the beta-adrenoreceptor antagonists metoprolol and oxprenolol: design and evaluation of systems for once-daily administration. Br J Clin Pharmacol 1985; 85: 69S-76S.
7. Gohel M Parikh and RK Shah NY: Osmotic drug delivery: An update. Pharmainfo Net 7(2): 47-50.
8. Bhatt P: Osmotic drug delivery systems for poorly soluble drugs. The Drug Delivery Companies Report Autumn Winter Pharma Ventures Ltd 2004; 26-29.
9. Ajay B, Prasada R and Vijaya RJ: Controlled-porosity osmotic pump tablets-an overview. IJPSR Journal 2010; 2(1): 114-26.
10. Sharma S: Osmotic drug delivery system. Pharmainfo Net 2008; 6(3).
11. Kojima H, Yoshihara K, Sawada T, Kondo H and Sako K: 2008.
12. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 3rd ed. Philadelphia, USA Churchill Livingstone Elsevier 99-102.
13. Gadwal P, Rudrawal P, Ahamad D and Ahmed A: A review on osmotically regulated devices. International Journal of Pharmacy & Life Sciences 2010; 1(6): 302-12.
14. DiMatteo MR and DiNicola DD: Achieving patient compliance: the psychology of the medical practitioners role. New York Pergamon press 1982.
15. Vincent M, Joerg O, Nicoletta L and Robert G: Oral osmotically driven systems: 30 years of development and clinical use. European Journal of Pharmaceutics and Biopharmaceutics 2009; 73: 311-23.
16. Higuchi T and Leeper HM: Improved osmotic dispenser employing magnesium sulphate and magnesium chloride. US Patent 1973; 3760804.
17. Theeuwes F, Swanson D, Wong P, Bonsen PV, Heimlich, K, Kwan KC: Elementary osmotic pump for indomethacin. Journal of Pharmaceutical Sciences 1983; 72(3): 253-58.
18. Zentner GM, Rork GS and Himmelstein KJ: Osmotic flow through controlled porosity films, an approach to delivery of water soluble compounds. Journal of Controlled Release 1985; 1: 269-82.
19. S Rose and JF Nelson: Aust J Exp Biol Med Sci 1955; 33: 415.
20. RL Jerzewski and YW Chien: Osmotic drug delivery, in treatise on controlled drug delivery. fundamentals, optimization, applications (a. kydonieus, ed.), marcel dekker. New York 1992; 225-53.
21. T Higuchi: US Patent 3,760,805 (1973). & T. Higuchi and HM: Leeper, US Patent 3,760,804 (1973) & T. Higuchi and H. M. Leeper, U.S. Patent 1985; 3: 995-31.
22. SK Chandrasekaran, F Theeuwes and SO Yum: The design of controlled drug delivery systems, in Drug Design. New York 1979; 8: 134-65.
23. Martin A, Bustamante P and Chun B: Physical Pharmacy: Physical chemical principles in the pharmaceutical sciences. 4th Ed Phila Lea and Febiger 1993; 116-18.
24. Li X and Jasti BR:. Osmotic controlled drug delivery systems, In: design of controlled release of drug delivery systems. McGraw Hill 2006; 203-29.
25. Santus G and Baker RW: J Control Release 1995; 35: 2.
26. Stuti G, Ravindra PS and Rohitashva S: International Journal of Comprehensive Pharmacy 2011; 6: 1.
27. Sharma S, Singh SP, Bhardwaj S, Gaurav K and Gupta GD: Latest Reviews Internet.2008; 6.
28. B Lindstedt, G Ragnarsson and J Hjartstam: Osmotic pumping as a release mechanism for membrane-coated drug formulations. International Journal of Pharmaceutics. 1989; 56(3): 261-68.
29. LA Seminoff and GM Zentner: "Cellulosic coating. US Patent 1992; 5: 126-46.
30. JL Jensen, LE Appel, JH Clair and GM Zentner: "Variables that affect the mechanism of drug release from osmotic pumps coated with acrylate/methacrylate copolymer latexes. Journal of Pharmaceutical Sciences 1995; 84(5): 530-33.
31. F Theeuwes: "Elementary osmotic pump. Journal of Pharmaceutical Sciences 1975; 64(12): 1987-91.
32. Tanmoy Ghosh and Amitava Ghosh: Journal of Applied Pharmaceutical Science 2011; 1(2): 38-49.
33. Rastogi SK, Vaya N and Mishra B: East Pharm 1995; 38: 79-82.
34. T Ghosh and A Ghosh: "Drug delivery through osmotic systems—an overview. Journal of Applied Pharmaceutical Science 2011; 2: 38-49.

35. S Gupta, RP Singh, R Sharma, R Kalyanwat and P Lokwani: Osmotic Pumps: A Review. Pharmacie Globale IJCP 1(6): 2011.
36. Zentner GM, Rork GS and Himmelstein KJ: US Patent No 1990; 4968507.
37. GM Zentner, GS Rork and KJ HimmelsteinL "Osmotic flow through controlled porosity films: an approach to delivery of water soluble compounds. Journal of Controlled Release 1985; 2: 217-29.
38. GM Zentner, GS Rork and KJ Himmelstein: "Controlled porosity osmotic pump. US Patent 1990; 4: 968-07.
39. M Kelbert and SR Bechard: "Evaluation of a cellulose acetate (CA) latex as coating material for controlled release products. Drug Development and Industrial Pharmacy 1992; 18(5): 519-38.
40. Ajay B, Prasada R and Vijaya RJ: Controlled-porosity osmotic pump tablets-an overview. JPRHC 2010; 2(1): 114-26.
41. Khavare NB, Fatima SD, Nanjundaswamy NG: A review on key parameters and components in designing of Osmotic Controlled Oral Drug Delivery Systems. Indian Journal of Novel Drug delivery 2010; 2(4): 122-31.
42. Thakor RS, Majumdar FD, Patel JK and Rajaput: Review GC. Osmotic drug delivery systems current scenario. 2010; 34: 771-75.
43. EM Rudnic, BA Burnside and HH Flanner: Patent 2000.
44. Vyas SP and Khar RK: Controlled drug delivery: concept and advances. Vallabh Prakashan New Delhi 2001; 477-01.
45. Higuchi T and Leeper HM: Improved osmotic dispenser employing magnesium sulfate and magnesium chloride. US Patent 1973.
46. Rajagopal K, Nallaperumal N and Venkatesan S: Lipids in Health and Disease 2011; 10: 51.
47. Srikonda Sastry and Kotamraj Phanidhar: Barclay brian, osmotic controlled drug delivery system, in li xiaoling, jastibhaskara r (eds), design of controlled release drug delivery systems, McGraw-Hill Companies INC New York 2006; 203-29.
48. T Higuchi and HM Leeper: Improved osmotic dispenser employing magnesium sulfate and magnesium chloride. US Patent 1973; 3: 760-04.
49. JH Guo: Effects of plasticizers on water permeation and mechanical properties of cellulose acetate: anti-plasticization in slightly plasticized polymer. Drug Development and Industrial Pharmacy 1993; 19(13): 1541-55.
50. C Bindschaedler, R Gurny and E Doelker: "Mechanically strong films produced from cellulose acetate latexes. Journal of Pharmacy and Pharmacology 1987; 39(5): 335-38.
51. JH Guo: "An investigation into the formation of plasticizer channels in plasticized polymer films. Drug Development and Industrial Pharmacy 1994; 20(11): 1883-93.
52. GA McClelland, SC Sutton, K Engle and GM Zentner: "The solubility-modulated osmotic pump: in vitro/in vivo release of diltiazem hydrochloride. Pharmaceutical Research1991; 8(1): 88-92.
53. Verma RK, Mishra B and Garg S: Osmotically controlled oral drug delivery. Drug Dev Ind Pharm 2000; 26: 695-08.
54. NK Jain: Advances in controlled and novel drug delivery, CBS Publisher & distributor, first edition. Page 20.
55. S Rose and JF Nelson: "A continuous long-term injector. The Australian Journal of Experimental Biology and Medical Science 1995; 33(4): 415-19.
56. Gadwal P and Rudrawal P: International Journal of Pharmacy & Life Sciences 2010; 1(6): 302-12.
57. T Higuchi and HM Leeper: US Patent 399.
58. T Higuchi: "Osmotic dispenser with collapsible supply container. US Patent 760-05; 3: 1973.
59. T Higuchi and HM Leeper: "Osmotic dispenser with means for dispensing active agents responsive to osmotic gradient.US Patent 1976.
60. F Theeuwes and T Higuchi: Osmotic dispensing device for releasing beneficial agent.US Patent 1974.
61. Higuchi: US Patent 3995631; 1976.
62. F Theeuwes and SI Yum: "Principles of the design and operation of generic osmotic pumps for the delivery of semisolid or liquid drug formulations. Annals of Biomedical Engineering 1976; 4(4): 343-53.
63. F Theeuwes: "Osmotic system for delivering selected beneficial agents having varying degrees of solubility. US Patent 4111201; 1978.
64. ALZET Osmotic pumps http://www.alzet.com/research_applications.
65. Khanna SC: Therapeutic system for sparingly soluble active ingredients. US Patent 4992278; 1999.
66. Sungthong Jeans, Sriamornsak P and Puttipipatkhachorn S: Design and evaluation of floating multi-layer coated tablets based on gas formation. Eur J Pharm Biopharm 2008; 69: 255-63.
67. Iannuccelli V, Coppi G, Bernabei MT and Cameroni R: Air compartment multiple-unit system for prolonged gastric residence. Part I. Formulation study. Int J Pharm 1998; 174: 47-54.
68. Theeuwes F: Elementary osmotic pump. J Pharm Sci 1975; 64: 1987-91.
69. Theeuwes F, Swanson D, Wong P, Bonsen P, Place V, Heimlich K and Kwan KC: elementary osmotic pump for indomethacin. J pharm Sci 1983; 72: 253-58.
70. Rawat D, Prabakaran P, Singh P, Kanaujia KS, Jaganathan P and Suresh Vyas: Int Journal of Pharmaceutics 2004; 284: 95-08.
71. B Mishra, BK Makes and C Sankar: Ind J Pharm Sci 2006; 68(1): 85-87.
72. Liu L, Ku J, Khang G, Lee B, Rhee JM and Lee HB: Nifedipine controlled delivery by sandwiched osmotic tablet system. J Control Release 2000; 68: 145-56.
73. HB Lee, L Liu, J Ku, G Khang, B Lee and JM Rhee: J Control Release 2000; 68: 145-56.
74. Tanmay G and Amitava G: Drug delivery through osmotic system: An overview. Journal of Applied Pharmaceutical Sciences 2011; 1(2): 38-49.
75. Khan I, Arjariya P, Ratnakar D and Farheen F: A review: an article of importance in its field of osmotic pump controlled drug delivery system. Indo American Journal of Pharmaceutical Research 2013; 3(4): 3147-57.
76. Dong L, Shafi K, Wan J and Wong P: A novel osmotic delivery system: L-OROS softcap. proceedings of the 27th international symposium on controlled release of bioactive materials. Controlled Release Society 2000.
77. Dong L, Wong P and Espinal S: L-oros hardcap, a new osmotic delivery system for controlled release of liquid formulation. proceedings of the 28th international symposium on controlled release of bioactive materials. Controlled Release Society 2001; 23-27.
78. Liu L, Ku J, Khang G, Lee B, Rhee JM and Lee HB: Nifedipine controlled delivery by sandwiched osmotic tablet system. J Cont Rel 2000; 68: 145-56.
79. R Sareen, N Jain and D Kumar: Curr Drug Deli 2012; 9(3): 285-96.
80. R Gupta, R Gupta, BPK Rathore and S Garvendra: Int J Ph Sci 2009; 1(2): 269-75.

81. Parmar NS and Vyas SK: Advances in controlled and novel drug delivery. CBS Publishers New Delhi 2008; 28-29.
82. Swarbrick J and Boylan CJ: Encyclopedia of pharmaceutical technology. Marcel Decker Inc New York, 4th Edition 310; 1991.
83. Chein YW: Novel drug delivery systems: fundamentals developmental concept and biomedical assessments. Dekker Publisher New York 1982; 59-64.
84. Santus G and Baker RW: Osmotic drug delivery: a review of patent literature. Controlled Release 1995; 35: 1-2.
85. L Liu and X Wang: Eur J Pharm Biopharm 2008; 68(2): 298-02.
86. GX Yang, HG Zhang, W Lie, B Peng, DZ Liu and SW Pan: Chem Pharm Bull 2006; 54(4): 465-69.
87. Verma RK, Krishna DM and Garg S: Formulation aspects in the development of osmotically controlled oral drug delivery systems. J Cont Rel 2002; 79: 7-27.
88. S Padmapriya, V Ravichandran and V Suba: Int J of Research in Pharmaceutical and Biomedical Sciences 2013; 4(3): 810-21.
89. R Sareen, N Jain and D Kumar: Curr Drug Deliv 2012; 9(3): 285-96.
90. Edavalath S, Shivanand K and Prakasam K: Formulation development and optimization of controlled porosity osmotic pump tablets of Diclofenac Sodium. Int J of Pharm and Pharma Sci 2011; 3: 438-46.
91. Zentner GM, Rork GS and Himmelstein KJ: The controlled porosity osmotic pump. J Cont Rel 1985; 1: 269-82.
92. F Theewes, PSL Wong, TL Burkoth, DA Fox and PR Bicek: Colonic drug absorption and metabolism. Marcel Decker New York 1993; 137-58.
93. Madhavi BB, Nath AR, Banji D, Ramalingam R, Madhu MN and Kumar DS: Osmotic drug delivery system: a review. Pharmakine 2009; 2: 5-14.
94. Verma RK and G Sanjay: Current status of drug delivery technologies and future direction. Pharm Tech On line 2001; 25: 1-14.
95. Khavare NB, Fatima SD and Najundaswamy NG: A review on key parameters and components in designing of osmotic controlled oral drug delivery systems. Indian Journal of Novel Drug delivery 2010; 2(4): 122-31.
96. Thakor RS, Majmudar FD, Patel JK and Rajput GC: Osmotic drug delivery systems current scenario. J of Pharm Res 2010; 3(4): 771-75.
97. Verma RK, Mishra B and Garg S: Osmotically controlled oral drug delivery. drug dev ind pharm 2000; 26: 695-08.
98. good wr and lee pi: membrane-controlled reservoir drug delivery systems, in langer rs, wise dl (eds). Medical Applications of Controlled Release Boca Raton CRC Press 1984; 1-39.
99. Gaebler F: Laser drilling enables advanced drug delivery systems. Coherent article for. Pharma Manufacturing Jan 2007; 1-7.
100. Khanna SC: Therapeutic system for sparingly soluble active ingredients. Ciba-Geigy Corporation Ardsley NY US Patent 4992278; 1997.
101. Okimoto K, Ohike A and Ibuki R: Design and evaluation of an osmotic pump tablet (OPT) for prednisolone: a poorly water soluble drug using (SBE)7m-beta-CD. Pharm Res 1998; 15: 1562-68.
102. Eckenhoff B, Theeuwes F and Urquhart J: Osmotically actuated dosage forms for rate-controlled drug delivery. Pharm Technol 1987; 11: 96-105.
103. RK Verma, DM Krishna and S Garg: "Formulation aspects in the development of osmotically controlled oral drug delivery systems. J of Controlled Release 2002; 1(3): 7-27.
104. C Chen, D Lee and J. Xie: "Controlled release formulation for water insoluble drugs in which a passageway is formed in situ. US patent 5736159; 1998.
105. Ozdemir N and Sahin J: Design of a controlled release osmotic pump system of ibuprofen. Inter J. Pharmaceutics 1997; 158: 91-97.
106. Swanson DR, Barclay BL, Wong PS and Theeuwes LF: Nifedipine gastrointestinal therapeutic system. American J Med 1987; 83: 3-9.
107. Choudhury PK, Ranawat MS, Pillai MK and Chauhan CS: Asymmetric membrane capsule for osmotic delivery of flurbiprofen. Acta Pharm 2007; 57: 343-50.
108. Philip AK and Pathak K: In situ formed phase transited drug delivery system of ketoprofen for achieving osmotic control and level *in-vitro in-vivo* correlation. Ind J pharm Sci 2008; 70: 745-53.
109. Mahalaxmi R, Sastri P, kumar R, Kalra A, Kanagale P and Narkhede: Enhancement of dissolution of glipizide from controlled porosity osmotic pump using a wicking agent and a solubilizing agent. Int J Pharm Tech Res 2009; 1: 705-11.
110. Kumar Pramod, Singh Sanjay and Mishra Brahmeshwar. Development and evaluation of elementary osmotic pump of highly water soluble drug: tramadol hydrochloride. Current Drug Delivery 2009; 6: 130-39.
111. Rajeshri Wakode and Varma MM: Once a day osmotic drug delivery system for highly water soluble Pramipexole. J Chem Pharm Res 2010; 2: 136-46.
112. Mothilal M, Damodharan N, Lakshmi KS, Sharanya VB and Srikrishna T: Formulation and *in-vitro* evaluation of osmotic drug delivery system of metoprolol succinate. Int J Pharm Pharm Sci 2010; 2: 64-68.

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