A BRIEF REVIEW ON OSMATIC PUSH TABLET

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***Abstract*- People who have used traditional drug delivery methods know that the drug is released right away, and that the concentration of the drug at the target spot can't be controlled or kept high for a long time. Controlled drug delivery methods let you choose where the drug is released. The most promising method for controlled drug transport is an osmotic pump. These methods are used for both implanting and giving medicine by mouth. Osmotic pumps have a core inside that has drugs and osmogens in it, and a layer on the outside that lets some things through but not others. The core gets bigger as it takes in water, which forces the drug solution out through the delivery ports. The rate at which osmotic pumps release drugs is not affected by the pH or the way water moves in the breakdown medium. The Rose-Nelson pump, the Higuchi-Leeper pumps, the Alzet and Osmet systems, the basic osmotic pump, and the push-pull system are all examples of how osmotic systems have changed over time. The controlled porosity osmotic pump and systems based on asymmetric membranes are two new developments. This essay talks about the basic idea behind osmosis, the different types of pumps that can be made, their pros and cons, and the goods that are sold that use this system.**

***Keywords*: Conventional, Osmotic Pump, etc.**

Introduction

Taking drugs by mouth is a useful way to give them because it is cheap and easy for the patient to follow. But most drug delivery systems don't control when the drug is released and let it out right away. Different things, like the physical qualities of the drug, the presence of excipients, physiological factors like food or not, the pH of the gastrointestinal (GI) tract, GI movement, and so on, can have a big effect on the rate and amount of drug absorption from standard forms. To get around these problems, experts have been working on making a new drug delivery system (NDDS). [(1,2,3)]

If you put pressure on a barrier that lets some water through but not others, you have osmosis [(4)]. The content of the liquid is different on both sides of the semipermeable barrier, which makes pressure. Water molecules can pass through this membrane, but most salt molecules can't. This is because the membrane permeability is limited. The pressure put on the side with more liquid to stop it from moving is known as the osmotic pressure [(5)]. Osmosis is also known as the moving of water across a semi-permeable surface from a place where the concentration is greater to a place where the concentration is lower [(6)].

Over the past ten years, getting new drugs to market has been hard for the pharmaceutical industry. Besides that, the price of making a new drug product keeps going up and now costs more than US$800 M for each one. Drug transport study keeps coming up with new ways to treat and avoid both old and new diseases. On the other hand, drug delivery systems are very helpful because they offer better versions of current drugs that are better at getting into the body's circulation [(7-8)].

In modern times, osmotic pills have grown in size. The delivery hole is made by adding a leachable component to the covering. When the pill comes into touch with water, the parts that dissolve in water break down, creating an osmotic pumping system. Later, the water moves into the core through the microporous membrane. This makes an osmotic gradient, which controls how much of the drug is released. According to definition 6/17, osmosis is when a solvent moves freely from a solution with less solute to a solution with more solute through a perfect semipermeable membrane that lets the solvent through but not the solute. The osmotic pressure is the force that is put on the side with more concentration to stop the flow of the solvent. People have recently come up with osmotic tablets that have a delivery opening made by adding a leachable component to the coating.

The water-solvent part split when the pill came into contact with the fluid, and the osmotic siphoning structure was created. After that, water moves into the core through the microporous membrane. This creates an osmotic difference that controls the drug's release. [(9-10)]

Controlled drug delivery methods let you choose when and where the drug is released. These kinds of systems can release the drug at a steady rate or a rate that changes over time. Because taking drugs by mouth is so convenient, oral controlled drug delivery systems are the most common type of controlled drug delivery systems. These dosing types have many benefits, including a drug level that stays almost the same at the site of action, no peak-valley changes, a lower amount of drug, fewer dosages, fewer side effects, and better patient compliance.

When a drug is released through the sublingual controlled release method, it usually stays between the minimum effective concentration (MEC) and maximum safe concentration (MSC) for a long time. This makes sure that the drug continues to work as a medicine should. [28]

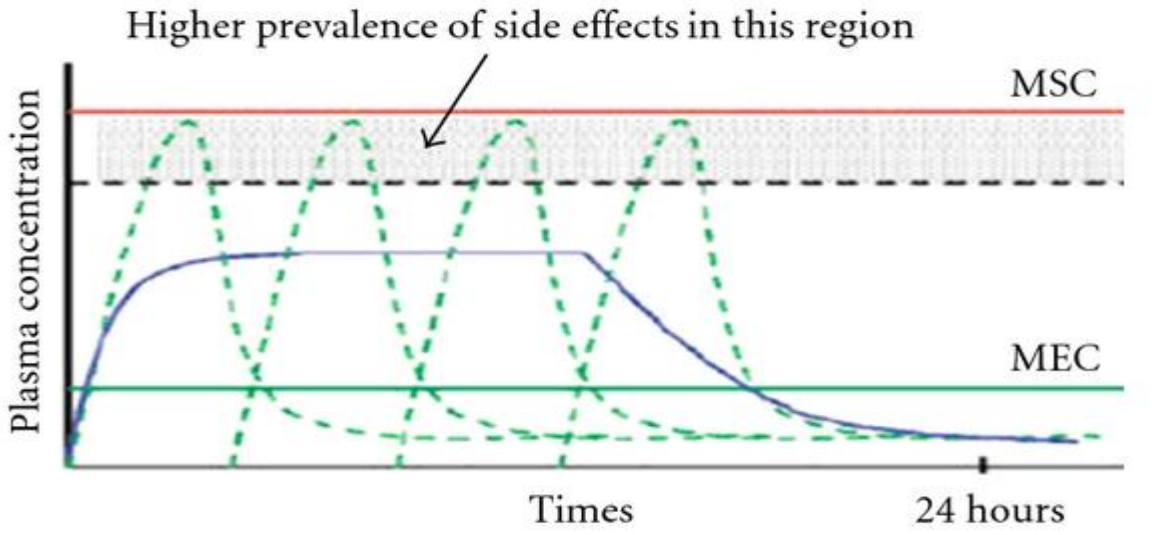

Figure 1 – Plasma concentration profile: for conventional dosage form and for controlled release dosage form.

Advantages [11]

1. Better patient compliance with fewer doses given more often.
2. With this method, it is possible to get faster release rates than with normal diffusion.
3. The osmotically controlled drug delivery method has a strong in vitro-in vivo association (IVIVC) within certain limits for drug release.
4. Higher safety limit for drugs with a lot of power.
5. Lessened the side effects.

Disadvantages [11,12]

1. In a basic osmosis system, the size of the hole is very important.
2. Food can have some effect on how drugs are released from the osmosis systems.
3. You can't get your therapy back if something bad happens out of the blue.
4. Getting used to things quickly.
5. It is hard to keep this system's purity and provide the stability it needs.

Basic components of osmotic System

A. Drugs

Osmotic systems work best with drugs that have a short cellular half-life (2–6 hours), are very strong, and are used to continue treatment. Osmotic transport is used to make drugs like Diltiazem HCl, Carbamazepine, Metoprolol, Oxprenolol, Nifedipine, Glipizide, verapamil, and others. Drugs should not be either very highly soluble or very badly soluble in order to work in this system. They should also be strong enough for this reason. [14-15]

B. An Osmotic Agent

Other names for osmotic agents are osmogents and osmogogens. They are what make the osmotic pressure in the osmotic transport system. Because some drugs aren't very soluble, they are released slowly. To speed up this process, osmotic agents are added to the mixture. The rate of drug release speeds up because these substances create a large difference in osmotic pressure within the osmotic system. [16] Osmogents can be broken down into several groups, including those that dissolve in water and are inorganic acids (magnesium chloride or sulfate, lithium, sodium, or potassium chloride, sodium or potassium hydrogen phosphate), those that dissolve in water and are organic acids

(sodium and potassium acetate, magnesium succinate, sodium benzoate, sodium citrate, sodium ascorbate), and those that dissolve in water and are amino acids and organic polymers. Polymeric osmogents are mostly used to make osmotically controlled drug delivery systems and other devices that let drugs that aren't easily dissolved be released in a controlled way. Osmotic pressures are very high for concentrated solutions of soluble solutes that are often used in controlled release recipes. They can be as low as 30 atm for sodium phosphate and as high as 500 atm for a mixture of lactose and fructose. High water flows can happen through semipermeable barriers because of these osmotic forces [17–18].

C. Semipermeable Membrane

As the osmosis system membrane selectively permeable, the polymer should also be selectively permeable, so that only water can pass through and solutes should not [19]. When making an osmotic pump, cellulose acetate is the material that is used most often and in large amounts. It comes in different types of acetyl content [20]. Most of the time, grades with 32% and 38% acetyl content are used. The amount of acetyl is based on the degree of substitution, which is the average number of hydroxyl groups that are changed by replacing groups. cellulose esters, such as diacetate, propionate, cellulose acetate, triacetate, and cellulose acetate butyrate, are also used for this reason. Ethers of cellulose, like ethyl cellulose, can also be a part of this [21-22].

Many different types of polymers can be used to make semipermeable films. These include cellulose derivatives, agar acetate, amylose triacetate, betaglucan acetate, poly(orthoesters), poly acetals, selectively permeable poly(glycolic acid), poly(lactic acid) derivatives, and Eudragits. When choosing semipermeable plastics, permeability is the most important thing to look at. [28]

D. Hydrophilic and Hydrophobic Polymers

There are a lot of different kinds of polymers that are used to help make drug-containing matrix cores. To get a more controlled release, compounds that dissolve quickly in water can be trapped in matrices that don't like water, and compounds that dissolve slowly in water can be caught in matrices that like water. Most of the time, osmotic pumps for water-soluble drugs have been made with mixes of both hydrophilic and hydrophobic polymers. The choice is made based on how well the drug dissolves and how much and how fast it will come out of the pump.

They are either swellable or not swellable plastics. Mostly, pumps that hold drugs that dissolve slowly in water are made of swellable polymers. The non-swellable polymers are used when the drugs are very water-soluble because the swelling polymers raise the atmospheric pressure inside the pump. Because they can increase osmotic pressure, ionic hydrogels like sodium carboxymethyl cellulose are the best ones to use. By adding these polymers to the formulas, it is possible to get more precise controlled release of the drugs. For this, you can use hydrophilic polymers like hydroxy ethyl cellulose, carboxy methyl cellulose, hydroxy propyl methylcellulose, high-molecular-weight poly (vinyl pyrrolidone), and hydrophobic polymers like ethyl cellulose and wax types. [28]

E. Wicking Agents

If a substance can pull water into the open network of a delivery device, it is called a wicking agent. There are substances called washing agents that help the drug make more touch with the watery fluid that is coming in. When the washing agent is used, it speeds up the rate at which the drug is released from its opening. One type of washing agent doesn't swell and the other type does. Physisorption with water is one of the things that makes them unique. Physisorption is a type of absorption in which molecules of the fluid can stick to the surface of the wicking agent. This is possible because the surface of the wicking agent and the adsorbed molecule can interact with each other using Van der Waals forces. It's the job of the wicking agent to move water to surfaces inside the tablet's core, making paths or a network with more surface area. Such things as PVP, soluble silicon dioxide, and sodium lauryl sulfate are examples. [28]

F. Solubilizing Agents

For an osmotic drug delivery method to work, drugs that dissolve easily in water would have a high release rate that is of zero order. Because of this, many drugs that don't dissolve well in water aren't good options for osmotic transport. It is possible to change how easily drugs dissolve in the heart, though. Adding solubilizing agents to the core pill makes the drug dissolve much more easily.

Non-swellable solubilizing agents are classified into three groups:

I. Agents like PVP, poly (ethylene glycol) (PEG 8000), and β-cyclodextrin that stop medicines from crystallizing or work by complexing with drugs in some other way.

II. Something that forms micelles and has a high HLB value, like Tween 20, 60, and 80, polyoxyethylene or poly ethylene-containing surfactants, and other long-chain anionic surfactants like SLS.

III. Citrate esters, like alkyl esters and triethyl citrate, and how they mix with detergents that don't have a positive charge. Most people like it when complexing agents like polyvinyl pyrrolidone (PVP) and poly (ethylene glycol) are mixed with anionic detergents like SLS. [28]

G. Pore forming agent (Channelling agent)

Because pore-forming agents are present, a microporous barrier forms. A pore maker can also make walls with holes that are very small. As the system works, this pore maker leaches out and makes holes [23].

Controlled porosity or multi-particle osmotic pumps are made by this material. A pore-forming agent creates a barrier with very few pores. The microporous wall could be made on-site by a pore maker that is leached out as the system works. The things that make pores can be artificial or biological, solid or liquid. Alkaline metal salts are one type of pore material. alkaline earth metals like CaCl2 and calcium nitrate. Examples include NaCl, NaBr, KCl, potassium sulfate, potassium phosphate, and more. These include carbohydrates like sucrose, glucose, fructose, mannose, lactose, sorbitol, and mannitol, as well as diols and polyols like polyhydric alcohol, dibutyl phthalate, and polyvinyl pyrrolidone. It was ethanol and butanol that were used as the volatile pore formers. To make the pores, glycerol and water were used, which are not flammable. It shouldn't be harmful, and when they're taken away, pathways should form. [24-25]

H. Coating Solvent

The main job of the liquid system is to move the polymer (which is broken up or mixed) and other additives to the top of the material. Different kinds of neutral organic or mineral solvents are used to make a polymeric solution.(26) The right fluid should be used to make a polymeric membrane. You can get a number of different chemical and mineral solvents. It is important that solvents are safe and don't change the chemical makeup of polymers. They should also be able to dissolve polymers fully. These are some examples of solvents: ethyl acetate, butyl alcohol, carbon tetrachloride, ethanol, methanol, acetone, and water. Solvents like acetone, ethanol, isopropyl alcohol, methylene chloride-methanol, acetone-water, and methylene chloride-methanol-water are mixed together. [27]

Preparation of tablet core

The usual Wet Granulation Process is used to make the tablet core of PPOPs. The needed amount of ingredients for the drug layer and the push layer are mostly sieved through a 30 mm sieve and then mixed separately, leaving out the lube. Some swellable spreading agent (PEO) is mixed with drug layer ingredients to make a wet mass.

After going through a 16-mesh sieve, it is dried in a hot air oven or a fluidized bed dryer. The dried pellets are then put through a 22-number sieve and mixed with oils. The same steps are used to make push layer granules, but a coloring agent is added to them to make them stand out from drug layer granules. When the push layer pellets are added, the drug layer is compressed with a force of 6.0±1.0 kN. The drug layer is compressed with a force of 0.5±0.2 kN. Using the right tools and changing the dies' surface area, you can make tablets of different sizes and shapes.

Coating of bilayer tablets

To make coating solution, add acetone solution to water solution with plasticizer (PEG) dissolved in it. The cellulose acetate is added to the mixture and mixed until a clear solution forms. The above blend also has colorants and opacifiers added to it. Hydroxypropyl methyl cellulose is a covering or polymer film maker that is used in coats. Standard automatic coaters are used to coat the tablets, and the core of the covered tablet is dried overnight at the right temperature.

Drilling of orifice

At the top of the drug layer, the covered tablets have holes made in them. Different drilling methods are used depending on the size that needs to be done. Orifices can be made by hand drilling, laser drilling, or using modified punches, which is also known as "incidence."

Types of Osmotic Pumps

1. Rose-Nelson Pump

The Australian scientists Rose and Nelson were the first to use osmotic drug transport. They made an implanted pump in 1955 so that drugs could be sent to the guts of sheep and horses. There are three rooms in the Rose-Nelson internal pump shown in Figure 2. There is a drug chamber, a salt chamber with solid salt, and a water chamber. A semipermeable barrier separates the water chamber from the salt chamber. Because of the difference in osmotic pressure across the barrier, water moves from the water chamber to the salt chamber. It's possible that the water flow makes the salt chamber bigger, which in turn makes the rubber cushion between the salt and drug chambers stretch. Eventually, the drug is pumped out of the device.

The main issue with Rose-Nelson pumps was that the osmosis action started as soon as water touched the semipermeable barrier. This meant that pumps had to be stored empty and water had to be added before they could be used.

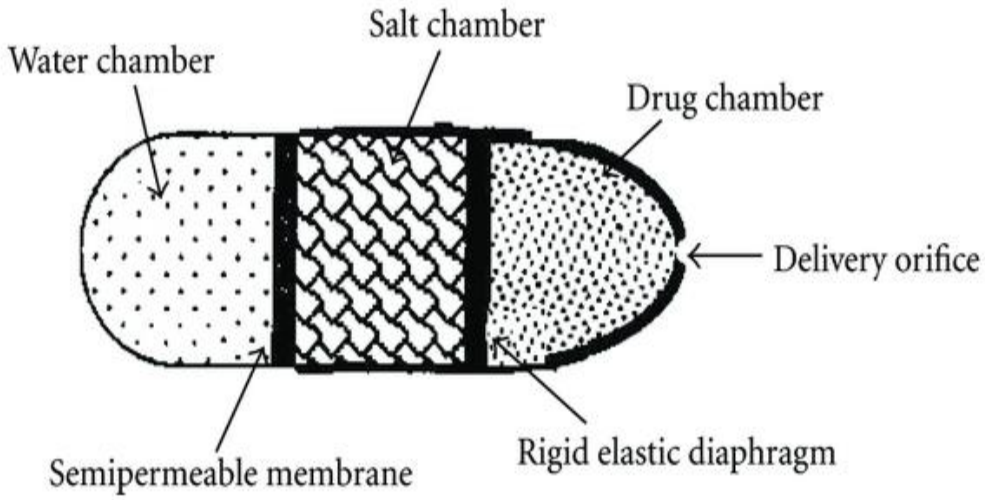

Figure 2: Rose Nelson Pump.

2. Higuchi-Leeper Osmotic Pump

A number of different versions of the Rose-Nelson pump have been suggested by Higuchi and Leeper. These designs are explained in US patents [46, 47], which are the first set of improvements to the Rose-Nelson pump that the Alza Corporation made. Figure 3 shows a picture of one of these pumps.

It's important to note that the Higuchi-Leeper pump doesn't have a water chamber. Instead, the device works by absorbing water from its surroundings. With this version, the device can be loaded with drug ahead of time and kept for a long time before it is used. Higuchi-Leeper pumps have a stiff body and a semipermeable membrane that is supported on a frame with holes in it. This type of pump usually has a salt cylinder that holds a fluid solution with too much solid salt in it. When the device is implanted or given, biological fluid from the area leaks into it through a porous and partially permeable membrane, dissolving the MgSO4. This creates osmotic pressure inside the device, which moves the moving separator toward the drug chamber to remove the drug from the device. It is often used for medical purposes. Animals have this kind of pump put inside their bodies so that medicines or growth hormones can be given to them.

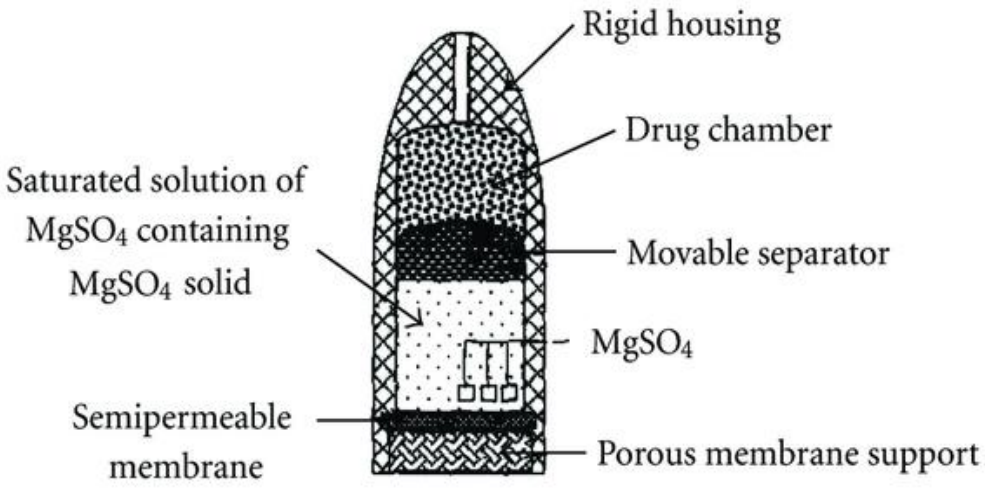

Figure 3: Higuchi-Leeper osmotic pump.

3. Pulsatile release osmotic pump

Using the Higuchi Leeper pump to achieve pulsed delivery is possible; these changes are shown and explained in Figure 4. Poisoned drug release is made possible by cutting a hole in a pliable material that bends when osmotic pressure is applied. Once a certain vital pressure is reached, the opening opens up and the drug is released in pulses. The pressure

then drops, which closes the opening. The cycle starts again, delivering the drug in a pulsed way. When the critical amount of osmotic pressure is not present, the opening should be small enough to close up most of the way. [28]

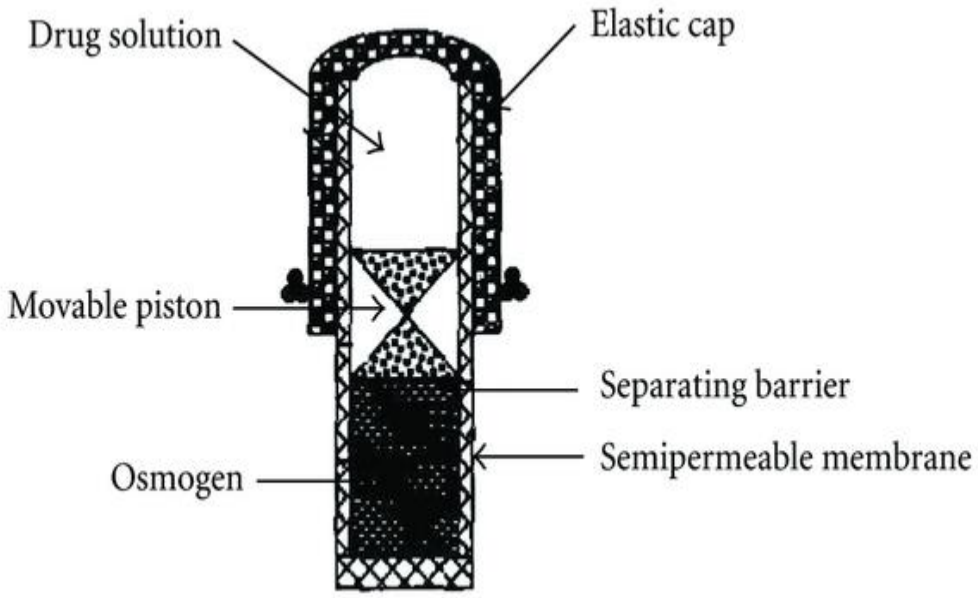

Figure 4: Pulsatile release osmotic pump.

Conclusions

For the past twenty years, push-pull osmotic pump tablets have been used as an important controlled drug delivery method. PPOS are used as a drug delivery method to show less food contact, which usually happens with drugs that don't dissolve well in food. This lets the drug be given only once a day, which makes treatment more tolerable and increases patient compliance. PPOP is better than EOP because it can release drugs that don't dissolve in water at the same rate. PPOPs have been successfully made and sold to deliver drugs for a wide range of conditions, including high blood pressure, angina, sugar, and once-a-day treatment for asthma and overactive bladder. This is despite worries about safety and huge progress in Novel Delivery methods.

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