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Push-Pull Osmotic Tablets - An Overview with Its Commercial Significance.

Prasoon P, Ramya Devi D, and Vedha Hari BN*.

Department of Pharmaceutical Technology, School of Chemical and Biotechnology, SASTRA University, Thanjavur-613401. Tamil Nadu, India

ABSTRACT

Delivery of drug by conventional systems are characterized by release of drug instantly, where the drug release and maintaining effective concentration at target site cannot be controlled. These patterns of dosing results in constantly fluctuating and unpredictable plasma concentration. For controlled drug delivery systems, controlled manner drug release can be achieved for prolonged period. There are many oral controlled drug delivery systems available in market, in which Osmotic Drug Delivery Systems (ODDS) have significant importance, as they have many advantages compared to others. Formulation and operation are easy in ODDS, improves patient acceptance with lowered frequency of dosing and provides prolonged therapeutic effectiveness with uniform blood concentration. In ODDS, the release of the drug is based on zero order kinetics which does not depend on the initial concentration and the physiological parameters of gastrointestinal (GI) tract like absence or presence of food, pH and temperature. The release properties can easily be studied and predicted from drug properties and dosage form available. Drug delivery through osmotic systems can be classified based on their design and the state of active ingredients. In this paper, various marketed osmotically controlled Push–Pull Osmotic Pumps (PPOPs) with their basic components and factors affecting have been discussed briefly. PPOP is a customized Elementary Osmotic pump, which can deliver both drugs with poor and high water solubility at a constant rate.

Keywords: Osmotic Drug delivery Systems, Gastro intestinal tract, Elementary Osmotic Pump, Push-Pull Osmotic Pump

*Corresponding author
INTRODUCTION

Controlled release through oral route has been preferred among all the novel drug delivery systems as they can deliver pharmaceutical agents in a controlled manner for a prolonged time period. The drug release from oral conventional systems is characterized by uncontrolled, instantaneous drug release, where maintaining an effective target site concentration is practically impossible. So, a significant variation in bioavailability of the active moiety from these systems occurs based on various factors such as physico-chemical properties of the drug, presence of excipients and different physiological factors of GI tract. This limitation can be overcome by a proper design by controlling or modulating the release of drug from the formulation. Major class of controlled drug delivery systems comes under reservoir, matrix or osmotic systems. But matrix and reservoir type posses various drawbacks such as, bioavailability variations due to various physiological factors like absence or presence of food, GI tract pH and its motility. Osmotic Drug Delivery Systems (ODDS) [1] have an unique advantage over other systems, as various physiological factors of gut lumen have no effect on delivery of the drug from the system and the prediction of release properties from known drug properties and formulation is easy. Drug releases from these dosage forms are not influenced by pH and other physiological factors to a large extend and by optimization of drug properties and the dosage form it is possible to modulate the drug release characteristics. Drug delivery in ODDS is follows controlled release pattern over a prolonged time period based on the mechanism of osmosis. There have been significant advances in the area of Oral osmotically Driven Systems (OODS) during the past three decades. The number of commercially available OODS has doubled in the last 10 years. Push pull osmotic pump is a type of modified Elementary Osmotic pump (EOP) by which the delivery of drug which are poorly water soluble and drugs which are water soluble can be achieved at a constant rate. EOP [1-8] is the most uncomplicated model of osmotic pump because, no special equipments or technology are needed for it. The EOP is composed of a monolayered tablet core composed of drug which is water soluble along with an osmotic agent or without it and as a whole is known as tablet core. The core tablet coated with a semipermeable membrane, when administered orally, absorbs water from GI tract into the core through the semipermeable membrane and the drug gets dissolved in it. The solution of drug is eliminated out through the delivery orifice at a constant rate until entire drug is released outside the system and follows zero order release kinetics until the osmotic pressure difference between outside and inside the semipermeable membrane attains equilibrium. Even though these osmotic pumps can deliver almost 60-80% of its constituents at a constant rate, it shows a shorter lag time of half an hour to 1 hour as these setup hydrates before zero order drug release from EOP [9]. And the major demerit of EOP is that, it is suitable only for the delivery of drugs which are water soluble [9,10]. This limitation is beaten, by developing a modified class of osmotic pump, Push-Pull Osmotic Pump (PPOP).

Push-Pull Osmotic Pumps

Push-pull osmotic pump (PPOP) or push-pull osmotic systems [1-8], is one of the widely used delivery system used to retard the release of poorly soluble drugs. They have been successfully manufactured and marketed to deliver drugs for various indications, such as
hyperglycemia, hypertension, angina, for once a day toms of urgency, frequency and in continuance and for asthma. PPOS have been proved as a mode of drug delivery to show reduction in food interaction, which is usually found in the case of poorly soluble drug substances [11], enables a once-a-day administration and hence improves treatment tolerability as well as patient compliance [9]. Push pull osmotic pump is a modified multi chamber Elementary osmotic pump, which can deliver both poorly water-soluble and highly water soluble drugs at a constant rate. PPOP looks like a typical two layered tablet with a semipermeable membrane. PPOP consist of a compressed bilayer tablet core, enveloped with a semipermeable membrane coat. One layer ie; drug layer (depict as the upper layer) consist of drug in a formulation along with polymeric osmotic agents for forming an in-situ drug suspension. The drug layer later absorbs water. Second layer, responsible for pushing the drug layer, is composed of osmotic and colouring agents, expansion polymer and tablet excipients. The two layers are developed separately and compressed together by tablet press to form a single, double layered tablet core. The tablet core is then coated with semi permeable membrane long with a flux regulator that regulates water flux into both layers surrounding the system. After coating and drying, a small hole is drilled through the membrane on the drug layer side of the tablet by a laser or mechanical drill. Various components of PPOPS are illustrated in Fig 1.

**Mechanism of Action of PPOPS**

Push-Pull Osmotic Pumps, on interaction with aqueous medium attracts water into the system and water is absorbed through the porous networks in the coat. On absorption of water, drug layer forms in-situ drug suspension and simultaneously push layer expand volumetrically and pushes out the drug suspension out through the drug delivery orifice as demonstrated in Figure 2.

![Components of PPOP](image-url)
Historical Aspects of Push-Pull Osmotic Pumps

The first report of developing bilayered PPOS was in 1980s [3,7] and it was first used for combination therapy in 1984 (Theeuwes et al, 1984) [7]. Pfizer developed PPOP for the delivery of Nifedipine in 1989 (Mishra et al, 2006) [7] and it became the most widely accepted delivery systems. PPOPs were successfully used for the treatment of hypertension from 1990 to 1995 and oxybutinin chloride PPOPs (Ditropan X) were developed in 1998 [12-14]. Eventhough the drugs which have been successfully manufactured and marketed using PPOP includes drugs for various indications such as hypertension, diabetis, angina and various other diasees, there were controversies regarding safety events [15] as seen with procardia XL. Clinical studies were done to examine the GI occlusions of PPOP in patients having certain disposition [16,17].

Basic Components of Push-Pull Osmotic Pumps

Drug

Poorly or moderately water soluble drugs with lesser biological half-life, used in extended treatment are perfect option for PPOPs. Drugs like Nifedipine, Glipizide, Prazosin Diltiazem, Verapamil, Oxybutininchloride,etc are successfully formulated as PPOPs [1-8].

Semi permeable membrane

Polymers which are water permeable but impermeable to solute particles (drug and excipients) can be used as semi permeable membrane in PPOPs. The membrane should be biocompatible and must be adequately rigid in order to retain its dimensional integrity during operation and must be sufficiently thick to withstand the pressure with the utyrate, cellulose system. Commonly used semipermeable membranes include cellulose esters like cellulose acetate and cellulose acetate phthalate [1-8, 18, 19].
Osmotic agent

Osmotic agents or osmogens are essential components of osmotic pumps, responsible for maintaining an effective concentration gradient through the membrane and act as a driving force for attracting water and help in maintaining an uniform drug distribution in the hydrated system. Commonly used osmotic agents in PPOPs are sodium chloride and potassium chloride [1-8].

Wicking agent

A wicking agent is defined as either swellable or non swellable material that has a tendency to attract water into the network of pores inside the osmotic system. They carry water from outside environment to tablet core surface and results in increased surface area by forming water channel. These materials are able to undergo physisorption with water. Commonly used wicking agents include titanium dioxide, silicon dioxide and polyvinylpyrrolidone (PVP) [1-8].

Plasticizers

Plasticizers have a significant role in the formation of coat and maintenance of structure. Plasticizers can increase the working capacity, permeability and flexibility of fluids. They are capable of changing the viscous and elastic nature of nature of the polymers and these changes can affect the polymeric film permeability significantly. Commonly used plasticizer for making low permeable films polyethylen glycol (PEG) and high permeable are diacetate, Tri ethyl citrate, Diethyl tartarate or Diacetin respectively [21].

Pore former

Pore formers are the agents used for the formation of microporous membrane by leaching of water soluble membrane substrate. Commonly used pore formers include alkaline metal salts like sodium chloride, potassium chloride, polyhyricalcohols and polyvinyl pyrrolidone[1-8].

Flux regulators

Permeability of the fluid can be regulated using flux regulators [1-8]. Hydrophilic flux regulators like PEG (300-600Da), polyalkylene glycol and polyhydric alcohols can be used to increase the flux whereas, hydrophilic flux regulators like diethyl phthalate or dimethoxy phthalate can be used to decrease the flux. Insoluble oxides or insoluble salts, which are considerably impermeable to water, can also be used as flux regulating agents [22].
Coating solvents

The role of solvent system is to dissolve or disperse the polymer and other additive and convey them to substrate surface. Inert inorganic and organic solvents that do cause any threats to the core composition and wall are used as coating solvent. They are used to dissolve or disperse the polymer and other additives together to the substrate surface. Less expensive solvents which are free from odour, taste, colour, toxicity and, with a rapid drying rate must be preferred as coating solvents. Commonly use coating solvents include isopropyl alcohol, dichloromethane, methanol, acetone, water and combination of various solvents in specified ratios can be used as coating solvents [22, 23].

Push-Pull Osmotic Tablet Preparation

Preparation of tablet core

Tablet core of PPOPs are prepared using conventional Wet Granulation Process. The required amount of drug layer ingredients and push layer ingredients are primarily sieved trough sieve number 30 and are separately blended except the lubricant. The alcoholic solution of swellable dispersing agent (PEO) is added to drug layer ingredients to form a damp mass. Then it is passed through a sieve number 16 mesh and is dried in hot air oven or fluidized bed drier. The dried granules are then sieved with 22 number sieve and is mixed with lubricants. Push layer granules are also prepared in a similar manner and a coloring agent is added to the push layer inorder to distinguish it from drug layer granules. The composition of drug layer is compressed with a tamping force of 0.5±0.2kN and is finally compressed with 6.0±1.0 kN after the addition of push layer granules. Tablet with the different shapes and size are obtained using the required punches and by varying surface area of the dies [24-29].

Coating of bilayer tablets

Coating solution is prepared by adding acetone solution to plasticizer (PEG) dissolved water solution. To the obtained mixture, cellulose acetate is added and is stirred until a clear solution is formed. Colourants and opacifiers are also added to the above mixture. Hydroxypropyl methyl cellulose is used in coats as polymer film formers or overcoats. Tablets are coated using standard automatic coaters and the coated tablet core is dried overnight at an optimum temperature [1, 2, 6, 7, 8, 24-33].

Drilling of orifice:

The coated tablets are drilled at the face of drug layer. Depending on the required scale different techniques are used for drilling. Orifice can be made using manual-drilling [34, 35], laser-drilling [36], or modified punches, so-called indentation [37, 38].
Advantages and Disadvantages of PPOPs

Advantages [39-46, 1-8]:

- Drugs with high water solubility and low water solubility can be delivered at constant rate.
- Delivery is independent of hydrodynamic condition, (ie); gastro intestinal motility.
- Drug release from system does not depend on GI pH of the environment.
- Drug release from the system is least affected by the presence of food in the GI tract.
- Can decrease the frequency of dosing.
- Delivery can be made delayed or pulsed, if required.
- Higher release rate can be achieved comparing to other diffusion-controlled drug delivery systems.
- Programmed and modulated release can be achieved.
- In vivo- in vitro correlation (IVIVC) is obtained at a higher extend.
- Greater success in treating chronic diseases..
- Side effects reduced to an extent.
- Improved patient compliance.
- Delivery rate independent of delivery orifice size within the limit.

Disadvantage [1-8, 47-50]:

- Controlled coating must be done to prevent the chance of defects in the film, which can result in dumping.
- Chance of gastro intestinal obstruction
- Orifice size is critical
- For making an orifice in the system special equipments are needed.
- Chances of ulcer.
- Cost of production high.

Factors Affecting the Release Rate from PPOPs

The parameters which are to be considered in designing a PPOP are as follows [7]:

1. Thickness of the membrane.
2. Osmotic pressure.
3. Types of membrane and characteristics.
4. Solubility.
5. Size of drug delivery orifice.
6. Wicking agent
7. Type and amount of plasticizer.
8. Concentration of swellable dispersing agent
9. Tablet Core
10. Presence of osmogen in both the drug layer and push layer
11. Drug: Polymer ratio and percentage weight gain in coating

**Thickness of the membrane**

Membrane thickness is an important parameter that controls the rate of penetration of water into the system. With suitable membrane materials, permeability of water into the system can be increased. By varying the thickness and varying the material, the release time of the active ingredients can be varied significantly [24-29].

**Osmotic pressure**

Osmotic pressure is an important factor that rate controlling factor [7, 24-29]. Atmospheric pressure created by osmogen can controlled the rate of drug release.

\[ F(z) = 1 - \frac{S}{p} \]

Where, \( S \) - solubility of the drug, \( F(z) \)-release of drug in zero order kinetics, \( p \)- density of tablet core

Van’t Hoff equation shows the relation between osmotic pressure and molar concentration of the solute in the solution:

\[ \pi = CRT \]

Where, \( \pi \)-osmotic pressure of solution, \( C \)- molar concentration of solute in the solution, \( R \)-Universal gas constant, \( T \)- Absolute temperature

**Type of membrane and characteristics**

Drug release from the osmotic system does not depend on the intestinal pH, position and intensity of agitation of GI tract to a large extend due to the presence of selective water permeable and as dissolution of drug core is separated from the gut environment. By adding plasticizers and hydrophilic flux regulators to polymers, membrane permeability can be increased. Plasticizers can increase the diffusion coefficient of water and hydrophilic flux regulators the sorption rate of water. Polyethylene glycols grades 300, 400, 600, 1500, 4000, and 6000(Ramakrishna, 2001) are generally used as hydrophilic flux [24-29,51].

**Solubility**

Solubility of the solute plays significant role in drug release rate [24-29]. Drugs which are poorly soluble and moderately soluble are the ideal candidates for PPOPs. For the delivery of drugs with poor solubility as suspension, swellable polymers and dispersing agents are added [52]. Solubility can also be modified by varying compression force of the tablet with drug and
excipients [53]. For example, compression along with cyclodextrin can enhance drug solubility [54]. Use of alternative salt forms of the drug, solubility can be modified to an extent [55].

Size of the delivery orifice

Orifice with optimum size must be drilled to achieve control over the drug release and for achieving zero-order delivery rate. In order to minimize the diffusion of solute through the orifice and to reduce hydrostatic pressure balance, its size must be smaller than the maximum range. Higher hydrostatic pressure may deform the delivery system and results in unpredictable drug release. There is no much influence of orifice diameter on release of drug in the size range between 0.5 to 1 mm diameters [25-29].

Wicking agent:

Wicking agent are used to increase the contact surface area by carrying water to surfaces inside the tablet core, and resulting formation of channels or network of increased surface area. Wicking agents in the PPOPs help to increase rate of release of drug through the orifice [29].

Type and amount of plasticizer

Hard and brittle polymers can be made soft, more flexible & their resistance to mechanical stress can be increased using plasticizer. Plasticizer can affect the viscous-elastic behavior of polymers and increase the permeability of the polymeric film. Water soluble plasticizers like PEG, HPMC, etc are used for creating a rapidly porous structure [56-58].

Concentration of swellable dispersing agent

An appropriate concentration of swellable dispersing agent (PEO) will results in the increase of drug release rate and release of the drug in a zero-order release profile [24].

Tablet Core

The tablet core composition has a significant role in drug release. The drug load, type and amount of PEO used, amount of sodium chloride used, and the drug layer is to swellable layer mass ratio includes core composition. Molecular weight of PEO in drug layer can significantly influence the rate of drug release. Drug loading and osmotic agent proportion has also affected on 24 hour release of the drug [25-28].

Presence of osmogen in both the Drug layer and Push layer

The PPOPs with different ratios of sodium chloride in both the drug layer and push layer are able to release 80 % of drug in a controlled manner upto 24 hours, whereas, the
formulations with osmotic agents only in push layer can release, less than 80% of the drug in 24 hours. Granules with best flow properties are use for optimization of formulation [24].

**Drug: Polymer ratio and percentage weight gain in coating**

Drug: polymer ratio and percentage weight gain in coating has direct influence on release rate in PPOPs. Almost 50% of drug is not released in PPOPs with 20% weight gain in 24 hours. A zero-order release of more than 80% of drug can be seen in formulations with 10% weight gain and 1:1 ratio of Drug: PEO in 24 hours with regression coefficient of 0.98 [24].

**Commercially available Push-Pull Osmotic Tablets and their Components**

**Commercially available Push-Pull Osmotic Tablets:**

Table (1) shows the list of commercially available PPOPs and general details.

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Trade name</th>
<th>Active ingredient</th>
<th>PPOP doses available(mg)</th>
<th>Half-life (hours)</th>
<th>Use</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Glucotrol XL</td>
<td>Glipizide</td>
<td>5,10</td>
<td>2-5</td>
<td>Treatment of hyperglycemia in patients with non-insulin dependent diabetes</td>
<td>Pfizer</td>
</tr>
<tr>
<td>2.</td>
<td>Ditropan XL</td>
<td>Oxybutinin chloride</td>
<td>5,10</td>
<td>12.4-13.2</td>
<td>Once a day treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and frequency</td>
<td>Janssen Pharmaceuticals</td>
</tr>
<tr>
<td>3.</td>
<td>Alpress LP</td>
<td>Prazosin</td>
<td>2.5-5</td>
<td>2-3</td>
<td>Treatment of hypertension</td>
<td>Pfizer</td>
</tr>
<tr>
<td>4.</td>
<td>Cardura XL</td>
<td>Doxazosin</td>
<td>4,8</td>
<td>22</td>
<td>Treatment of hypertension</td>
<td>Pfizer</td>
</tr>
<tr>
<td>5.</td>
<td>Covera HS</td>
<td>Verapamil</td>
<td>180,240</td>
<td>2.8-7.4</td>
<td>Treatment of hypertension and angina</td>
<td>GD Searle LLC</td>
</tr>
<tr>
<td>6.</td>
<td>Dynacirc CR</td>
<td>Isradipine</td>
<td>5,10</td>
<td>8</td>
<td>Treatment of hypertension</td>
<td>Glaxo Smith Kline LLC</td>
</tr>
<tr>
<td>7.</td>
<td>Procardia XL</td>
<td>Nifedipine</td>
<td>30,60,90</td>
<td>2</td>
<td>Treatment of high blood pressure and chest pain(angina)</td>
<td>Pfizer</td>
</tr>
</tbody>
</table>

** Excipients used in commercially available PPOPs**

Excipients used in PPOPs can be categorized based on following components:
- Drug layer components
- Push layer components
- Coating components

**Drug layer components**

Table (2) shows the list various excipients used in Drug layer of various PPOPs.
**Table (2): Drug layer components**

<table>
<thead>
<tr>
<th>Sl.No</th>
<th>Drug</th>
<th>Swellable dispersing agent/ Binder</th>
<th>Osmotic agent</th>
<th>Wicking agent</th>
<th>Sustained release swellable polymer</th>
<th>Lubricant</th>
<th>Stabilizer</th>
<th>Antioxidant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Glucotrol XL [59]</td>
<td>PEO</td>
<td>NaCl</td>
<td>TiO₂</td>
<td>Hypromellose</td>
<td>MgSt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Ditropan XL [60]</td>
<td>PEO</td>
<td>NaCl</td>
<td>TiO₂</td>
<td>Hypromellose</td>
<td>MgSt</td>
<td>Polysorbate 80</td>
<td>BHT (Butylated hydroxy toluene)</td>
</tr>
<tr>
<td>3.</td>
<td>Alpress LP [61]</td>
<td>PEO</td>
<td>NaCl</td>
<td>TiO₂</td>
<td>Hypromellose</td>
<td>MgSt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Cardura XL [62]</td>
<td>PEO</td>
<td>NaCl</td>
<td>TiO₂</td>
<td>Hypromellose</td>
<td>MgSt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Covera HS [63]</td>
<td>PEO/ Povidone/ Hydroxy ethyl cellulose</td>
<td>NaCl</td>
<td>TiO₂</td>
<td>Hypromellose</td>
<td>MgSt</td>
<td>Polysorbate 80</td>
<td>BHT</td>
</tr>
<tr>
<td>6.</td>
<td>Dynacirc CR [64]</td>
<td>PEO</td>
<td>NaCl</td>
<td>TiO₂</td>
<td>Hypromellose (or) HPMC</td>
<td>MgSt</td>
<td>Polysorbate 80</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Procardia XL [65]</td>
<td>PEO</td>
<td>NaCl</td>
<td>TiO₂</td>
<td>Hypromellose (or) HPMC</td>
<td>MgSt</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Push layer Components:**

Table (3) shows the list of excipients used in the Push layer of various PPOPs.

**Table (3): Push layer Components**

<table>
<thead>
<tr>
<th>Sl.No</th>
<th>Drug</th>
<th>Swellable dispersing agent/ Binder</th>
<th>Osmotic agent</th>
<th>Sustained release swellable polymer</th>
<th>Wicking agent</th>
<th>Lubricant</th>
<th>Colourant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Glucotrol XL [59]</td>
<td>PEO</td>
<td>NaCl</td>
<td>Hypromellose</td>
<td>TiO₂</td>
<td>MgSt</td>
<td>Red ferric oxide</td>
</tr>
<tr>
<td>2.</td>
<td>Ditropan XL [60]</td>
<td>PEO</td>
<td>NaCl</td>
<td>Hypromellose</td>
<td>TiO₂</td>
<td>MgSt</td>
<td>Synthetic iron oxide</td>
</tr>
<tr>
<td>3.</td>
<td>Alpress LP [61]</td>
<td>PEO</td>
<td>NaCl</td>
<td>Hypromellose</td>
<td>TiO₂</td>
<td>MgSt</td>
<td>Ferric oxide</td>
</tr>
<tr>
<td>4.</td>
<td>Cardura XL [62]</td>
<td>PEO</td>
<td>NaCl</td>
<td>Hypromellose</td>
<td>TiO₂</td>
<td>MgSt</td>
<td>Red ferric oxide</td>
</tr>
<tr>
<td>5.</td>
<td>Covera HS [63]</td>
<td>PEO/ Povidone/ Hydroxy ethyl cellulose</td>
<td>NaCl</td>
<td>Hypromellose</td>
<td>TiO₂</td>
<td>MgSt</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Dynacirc CR [64]</td>
<td>PEO</td>
<td>NaCl</td>
<td>Hypromellose (or) HPMC</td>
<td>TiO₂</td>
<td>MgSt</td>
<td>Red ferric oxide</td>
</tr>
<tr>
<td>7.</td>
<td>Procardia XL [65]</td>
<td>PEO</td>
<td>NaCl</td>
<td>Hypromellose (or) HPMC</td>
<td>TiO₂</td>
<td>MgSt</td>
<td>Red ferric oxide</td>
</tr>
</tbody>
</table>
Coating components:

Table (4) shows the list of components used in coating layer various PPOPs.

<table>
<thead>
<tr>
<th>Sl.No</th>
<th>Drug</th>
<th>Flux regulators</th>
<th>Plasticizer</th>
<th>Film overcoats</th>
<th>Colourants</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Glucotrol XL [59]</td>
<td>PEG</td>
<td></td>
<td>Hypromellose</td>
<td>Opadry colourants</td>
</tr>
<tr>
<td>2.</td>
<td>Ditropan XL [60]</td>
<td>PEG</td>
<td></td>
<td>Hypromellose</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Alpress LP [61]</td>
<td>PEG</td>
<td></td>
<td>Hypromellose</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Covera HS [63]</td>
<td>PEG</td>
<td></td>
<td>Hypromellose</td>
<td>Black iron oxide</td>
</tr>
<tr>
<td>6.</td>
<td>Dynacirc CR [64]</td>
<td>PEG</td>
<td>Propylene glycol</td>
<td>Hypromellose (or) HPMC</td>
<td>Yellow ferric oxide</td>
</tr>
<tr>
<td>7.</td>
<td>Procardia XL [65]</td>
<td>PEG</td>
<td></td>
<td>Hypromellose (or) HPMC</td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS

Push-pull osmotic pump tablets have been used successively as a significant controlled drug delivery system for the past two decades. PPOS are used as a drug delivery technology to show reduction in the food interaction, which is usually observed in the case of poorly soluble drug substances, enables a once-a-day administration and hence improves treatment tolerability as well as patient compliance. PPOP is advantages over EOP, as it can deliver both poorly water soluble and water soluble drugs at a constant rate. Even with safety concerns and enormous developments in the Novel Delivery systems, PPOPs have been successfully manufactured and marketed to deliver drugs for various indications, such as hypertension, angina, hyperglycemia, for once a day treatment of over active bladder and asthma.

REFERENCES


