INTRODUCTION

Conventional drug delivery systems have little or no control over the drug release, and effective concentration at the target site. This kind of dosing pattern may result in constantly changing, unpredictable plasma concentrations. The rate and extent of drug absorption from conventional formulations may vary greatly depending on the factors such as physico-chemical properties of the drug, presence of excipients, physiological factors such as presence or absence of food, pH of gastrointestinal tract and so on. However, drug release from oral controlled release dosage forms may be affected by pH, GI motility and presence of food in the GI tract. Osmotically controlled drug delivery offers several advantages than other controlled release system which include pH and gastric motility, independent drug delivery, predictable/programmable drug release and delivery of a combination of drugs. The system uses osmotic pressure for the delivery of drugs by a zero order. Osmotic drug delivery system has an excellent IVIVC and has very little effect of food on release rate. Therefore, in principle it is possible to achieve and sustain a drug plasma concentration within the therapeutic window of drugs, which reduces the side effects and frequency of administration considerably.

The oral osmotic tablet has many advantages, such as reducing risk of adverse reactions, improving patient compliance, in vivo predictability of release rate based on in vitro data, etc. Theeueuses introduced the elementary osmotic pump but it is only suitable for the water-soluble drugs. To overcome this limitation, various approaches were tried. One approach was the development of two-layer osmotic pump tablet whose core tablet consisted of two layers, one containing drug and the other an osmotic agent and an expanding agent. The disadvantage of this system was that a complicated side identification technology should be employed to ensure the orifice drilled on the surface of the drug layer after coating. Sandwiched osmotic pump tablet was developed with the elimination of side identification. Its core tablet consisted of a middle push layer and two attached drug layers. Two orifices were simply drilled on both sides of the surface after coating, which avoided side identification before drilling of that of two-layer osmotic pump tablet. However, all of those osmotic tablet systems have a common disadvantage:
a sophisticated technique is needed. To avoid additional production procedures, many researchers have attempted to invent a monolithic osmotic tablet system. Various attempts to increase the permeability of the coating have been reported, including plasticizers and coating, such as incorporating water-soluble additives in the coating\(^6\), and using multilayer composite coatings\(^7\). To further increase coating permeability, a new type of osmotic tablet was developed that consisted of a homogeneous tablet core coated with an asymmetric membrane film\(^8\). Another effective way to improve drug-released rate is to increase drug solubility. For some drugs, it is feasible to convert them into ionic substance by reacting with or adding alkali/acid. However, this method can only apply to a few drugs with special structures. However, for water-insoluble drugs, it is more suitable to release drugs in the form of suspension. Therefore, finding an appropriate polymer is pivotal to the success of this osmotic tablet.

There are various methods to prepare osmotic tablet but during these study, main focus will be given on two methods: (1) Elementary osmotic pump. (2) Controlled porosity osmotic tablet.

The elementary osmotic pump is a core tablet coated by semipermeable membrane with a micro-orifice drilled on the surface. The elementary osmotic pump is very simple in preparation and can deliver water-soluble drugs at an approximately constant rate up to 24 h. When this tablet is placed in an aqueous environment, the osmotic pressure of the soluble drug inside the tablet draws water through the semipermeable coating, forming a saturated aqueous solution inside the device. The membrane is non-extensible, and the increase in volume caused by the imbibition of water raises the hydrostatic pressure inside the tablet slightly. This pressure is relieved by a flow of saturated agent solution out of the device through the small orifice. Thus, the tablet acts as a small pump, in which water is drawn osmotically into the tablet through the membrane wall and then leaves as a saturated agent solution via the orifice. This process continues at a constant rate until the entire solid drug inside the tablet has been dissolved and only a solution-filled shell remains. This residual dissolved drug continues to be delivered, but at a declining rate, until the osmotic pressure inside and outside the tablet is equal. However, it was not
feasible for the delivery of drugs with low solubility, for the drugs dissolved insufficiently and settled in the bottom of the tablet. Therefore, researches were carried out to enhance the solubility of the drugs and to modify the performance of the semipermeable membrane⁹, but these methods were only practicable for a few kinds of drugs.

In controlled porosity osmotic tablet, drug release done through coating contains pores which are formed in situ. These water-soluble additives dissolve on coming in contact with water, leaving behind pores in the membrane through which drug release takes place. Drug release from these types of system is independent of pH and has been shown to follow zero-order kinetics. A controlled porosity wall can be described as having a sponge like appearance. Water soluble additives that can be used for this purpose consist of sodium chloride, sodium bromide, potassium chloride, potassium sulphate, potassium phosphate, calcium chloride, calcium nitrate, glucose, fructose, mannose, lactose, sorbitol, mannitol, dimethyl sulfoxide, nicotinamide, saccharides, amino acids, pentaerythritol, organic aliphatic and aromatic acids, including diols and polyols such as polyhydric alcohols and polyvinyl pyrrolidone, and other water-soluble polymeric materials. Erodible materials, such as poly(glycolic), poly(lactic) acid, or their combinations can also be used for the purpose of formation of pores in the membrane. The pores may also be formed in the wall prior to the operation of the system by gas formation within curing polymer solutions, resulting in voids and pores in the final form of the membrane. The pores may also be formed in the walls by the volatilization of components in the polymer solution or by chemical reactions in the polymer solution leading to evolution of gases prior to application or during application of the solution to the core tablets reformed resulting in the creation of the polymer foams serving as the porous wall from where the drug release can take place. This type of device has a number of potential advantages. First, drug is released from the whole surface of the device rather than from a single hole, which may reduce stomach irritation problems. Also, because the hole is formed by a coating procedure, no complicated laser-drilling unit is required. Blended polymers play an important role in developing a microporous controlled delivery system. There can be combined two types of polymers in the blended films: one is
remained in the end use, and another is removed as a pore forming agent to produce porous structure. The release of drug is dominated by the thickness of coating films, the level of water soluble components, the solubility of drug, and the osmotic pressure difference.\textsuperscript{10}

**Advantages of Controlled Drug Delivery System**

- Reduction in drug blood level fluctuations.
- Reduction in dosing frequency.
- Enhanced patient convenience and compliance.
- Reduction in adverse side effects.
- Avoidance of night time dosing.
- More uniform effect.