Yuan and Wu reported that cellulose acetate (CA) has been widely used to form rate-controlling membranes for osmotic systems. CA films are insoluble, yet semipermeable to allow water to pass through the tablet coating. The water permeability of CA membrane is relatively high and can be easily adjusted by varying the degree of acetylation. As the acetyl content in the CA increases, the CA film permeability decreases, and solvent resistance increases. The permeabilities of these films can be further increased by the addition of hydrophilic flux enhancers. Incorporation of plasticizer in CA coating formulation generally lowers the glass transition temperature, increases the polymer-chain mobility, enhances the flexibility, and affects the permeability of the film.¹¹

Lindstedt and coworkers reported that ethyl cellulose is also widely used in the formation of membranes for oral osmotic systems. However, the water permeability of pure ethyl cellulose membrane is very low that may result in slow release of drugs.¹²

Lindstedt and coworkers reported that drug release from osmotic systems coated with ethyl cellulose membrane can be enhanced by incorporation of water-soluble additives. Addition of HPMC in the coating composition improves the permeability of ethyl cellulose membranes. Tablet cores of potassium chloride coated with a mixture of ethyl cellulose and up to 24% of HPMC, were shown to release the contents mainly through osmotic mechanism.¹³

In another study by Appel and Zenter, urea was added to commercially available ethyl cellulose aqueous dispersion (Aquacoat) in an attempt to increase the release rates of potassium chloride and diltiazem chloride from osmotic tablets. It was found that the drug release from these systems is affected by coating thickness, plasticizer type and concentration, and pore former level.¹⁴
The use of eudragit acrylic latexes as membrane formers for osmotic systems has also been reported in the literature by Jensen et al. Potassium chloride tablets were coated with mixtures of eudragit RS30D and RL30D containing triethyl citrate or acetyl tributyl citrate as plasticizers and urea as a pore-forming agent. The release rate was most affected by the ratio of RS30D to RL30D and the level of urea was found to have effect on lag time and burst strength. The type of plasticizer and amount of pore former were also found to be critical for the desired release rates. The mechanism of release from the formulations containing acetyl tributyl citrate as plasticizer and 100% urea level (of total polymer solids) was found to be primarily osmotic and these formulations exhibited similar release rates in water and phosphate buffer saline pH 7.4.\textsuperscript{15}

Thickness of the membrane has a profound effect on the drug release from osmotic systems. The release rate from osmotic systems is inversely proportional to membrane thickness. Pellets of phenylpropanolamine coated with an aqueous ethyl cellulose based films were found to release the drug mainly through the mechanisms of osmotic pumping and diffusion. On studying the release as a function of coating thickness, Ozturk et al. found that as the coating thickness increased from 9 to 50 µm, the drug release decreased in an inversely proportional manner.\textsuperscript{16}

Thickness of the membrane in case of asymmetric coating was found to have insignificant effect on drug release. In a study by Herbig et al. release rates were found to be virtually unaffected by the overall membrane thickness in the range of 95–150 µm. The possible reason for this may be the unique structure of the asymmetric membrane coatings in which the porous substrate consists of open pores (void volume between 60 and 90%). Since most of resistance to the transport is the skin structure rather than the porous substrate of the asymmetric membranes, the thickness of the porous substrate had only a slight effect on the release kinetics.\textsuperscript{17}

The effect of different types of plasticizers (TA and polyethylene glycols) on the water permeation and mechanical properties of CA was reported by Guo. The water permeability of CA films was found to decrease with increasing plasticizer concentration.
to a minimum and then increases with higher concentration of plasticizer. Low plasticizer concentrations were found to decrease water permeability by their antiplasticization effect. This antiplasticization effect could be because of interaction between the polymer and the plasticizer molecules that decreased the molecular mobility of the polymer.\textsuperscript{18}

In a similar study, Guo investigated the effect of PEG-600 on the sucrose permeability, void volume, and morphology of CA films. The sucrose permeability was found to decrease with increasing PEG-600 concentration and increase dramatically when they were plasticized by over 30\% (w/w). The decrease in sucrose permeability at lower plasticizer concentration was attributed to the antiplasticization effect. The increase in sucrose permeability at higher plasticizer concentration was because of formation of plasticizer channels, results of which were confirmed by the void volume and scanning electron microscopic studies.\textsuperscript{19}

Liu et al. studied the influence of nature and amount of plasticizers on the properties of CA membrane including drug release profile, thermal properties, microporosity, and mechanical properties. Hydrophilic plasticizer (PEG-200) was found to increase the drug release, whereas hydrophobic plasticizer (TA) was found to decrease the drug release from osmotic pumps of nifedipine. Films plasticized with PEG developed completely porous structure after 24 h leaching, whereas films plasticized with TA retained their dense structure and porosity was observed only on the surface. At low plasticizer levels (0–5\% w/w), it was found that both the ultimate tensile strength and elastic modulus of dry membranes increased as the plasticizer level increased and there was no significant difference because of the nature of plasticizer. However, at higher plasticizer levels (5–40\% w/w), both tensile strength and elastic modulus of membranes decreased as plasticizer levels increased.\textsuperscript{20}

In another study by Okimoto et al. chlorpromazine (CLP) release from controlled porosity osmotic tablets was found to increase with decreasing amounts of TEC. Drug release was also found to be much faster in formulations containing PEG-400 as a
plasticizer than with TEC and was similar to that obtained without a plasticizer. It was concluded that PEG-400 is not a very effective plasticizer.\textsuperscript{21}

\textbf{Bindshaedler et al.} have described mechanically strong films produced from CA latexes. By proper choice of type of plasticizer and its content in the coating composition, membranes comparable with those obtained from organic solutions can be produced from CA latexes. Water-soluble plasticizers possessing some degree of volatility resulted in films that had high ultimate tensile strength and elasticity modulus. In the series of films prepared with cellulose latexes containing different types and amount of plasticizers, it was found that the films plasticized with volatile additives (ethylene glycol monoacetate and ethylene glycol diacetate) were nearly as strong as those resulting from evaporation of solution in acetone. The majority of volatile plasticizer evaporates during the processing of the film at 60 $^\circ$C. On the other hand, more permanent plasticizers (triethyl phosphate and diethyl tartarate) are retained in the film and yield membranes that are weak and less resistant. Thus, by proper selection of these volatile plasticizers, it is possible to balance two contradictory requirements, i.e. high mechanical strength of films and initial high amounts of plasticizer.\textsuperscript{22}

\textbf{Gondaliya and Pundarikakshudu} prepared and evaluated controlled porosity osmotic tablet of diltiazem hydrochloride. That bilayered tablet containing one push layer and other pull layer was prepared. Push pull tablet was coated with cellulose acetate (12\%) in solvent mixture of IPA and acetone (1:1). Suitable plasticizer (dibutyl phthlate, PEG 400) and pore forming agent (glycerine) was added to the coating solution in different amount. Push compartment chiefly contains sodium CMC, sodium chloride, carbopol 71G and MCC. And pull layer contains diltiazem HCL, NaCl, guar gum and MCC. The effect of concentration of NaCl and concentration of sodium CMC in the push compartment was also studied. Effect of pore former’s concentration on drug release was also evaluated. The influence of concentration and type of plasticizer (dibutyl phthlate, PEG 400) on the diltiazem HCl release rate was studied and concluded that release rate was found inversely proportional to concentration to concentration of hydrophobic plasticizer (dibutyl phthlate) and directly proportional to hydrophilic plasticizer(PEG 400).\textsuperscript{23}
Lin and Lee developed a microporous-controlled delivery system for theophylline via coating a blend of PCL and PEG on the surface of tablets, where PCL was the major component of film coating material and PEG was acted as a leachable pore-forming agent when contacting with an aqueous medium. Theophylline tablets were prepared by directly compressed by IR compressor. Tablets were then coated by dip coating method. The influences of the type of solvent, the amount of PEG, and the thickness of films on the mechanical and thermal properties of coating films and drug release performance were investigated. The mechanical data showed a decrease tendency as increase in the amount of PEG in the blends due to highly crystalline character of PEG. Slower evaporation rate of acetone than dichloromethane enhanced phase separation between PCL and PEG during film formation, and resulted in the pore size in films prepared from acetone larger than from dichloromethane. The release rate of coated tablets was increased by increasing the amount of pore-forming agent, and the corresponding values from tablets coated in dichloromethane were less than in acetone. Much denser structure and smaller pore size of films formed from dichloromethane contributed to this result. The release of drug from tablets coated in acetone showed a profile more close to a zero-order constant release profile.24

Rani et al. formulated osmotic tablets of diclofenac sodium and evaluated effect of various variables on drug release. Tablet mainly contains diclofenac sodium, MCC, KCl, potassium bicarbonate and SLS. Tablets were coated with 2% cellulose acetate in acetone contains castor oil (20% w/w of cellulose acetate) as plasticizer or contains PEG 400 (20%w/w of cellulose acetate) as a pore former. Orifice through the membrane was made by a microdrill on one side of tablet. Effect of various variables like effect of orifice size, stirring condition and pH of dissolution media was studied and concluded that drug release from osmotic tablet was independent of orifice size, stirring condition and pH of dissolution medium.25

Makhijia and Vavia prepared a controlled porosity osmotic pump which consists of an osmotic core with the drug surrounded by a semipermeable membrane. Controlled
The porosity of the membrane is accomplished by the use of different channeling agents in the coating. Sodium bicarbonate was used as the osmogent. The effect of different ratios of drug:osmogent on the in-vitro release was studied. Cellulose acetate (CA) was used as the semipermeable membrane. Different channeling agents tried were diethylphthalate (DEP), dibutylphthalate (DBP), dibutylsebacate (DBS) and polyethyleneglycol 400 (PEG 400). The effect of polymer loading on in-vitro drug release was studied. It was found that drug release rate increased with the amount of osmogent due to the increased water uptake, and hence increased driving force for drug release. This could be retarded by the proper choice of channeling agent in order to achieve the desired zero order release profile. Also the lag time seen with tablets coated using diethylphthalate as channeling agent was reduced by using a hydrophilic plasticizer like polyethyleneglycol 400 in combination with diethylphthalate. This system was found to deliver pseudoephedrine at a zero order rate for 12 h. The effect of pH on drug release was also studied. But no significant differences in the release profile were seen in different pH media.26

Lin and coworkers studied the influence of different plasticizers on the release of theophylline from microporous-controlled tablets. Three plasticizers, acetyltributyl citrate, castor oil, and triacetin, were included in this study. These plasticizers reduced the crystallinity of poly(ε-caprolactone) (PCL)/poly(ethylene glycol) (PEG)-blended films. The size of micropores formed in the presence of plasticizer was larger than those micropores formed in its absence. The fatty plasticizer, castor oil, altered the thermal and mechanical performance and pore size of films via soluble in PCL domain, which resulted in the release of theophylline from castor oil plasticized-coated tablets, which in turn enhanced and closed to a constant release pattern.27

Liu and Che formulated monolithic osmotic pump tablet by coating the indented core tablet compressed by the punch with a needle. Atenolol was used as the model drug, sodium chloride as osmotic agent and polyethylene oxide as suspending agent. Ethyl cellulose was employed as semipermeable membrane containing polyethylene glycol 400 as plasticizer for controlling membrane permeability. The formulation of atenolol osmotic pump tablet was optimized by orthogonal design and evaluated by similarity
factor (f2). The optimal formulation was evaluated in various release media and agitation rates. Indentation size of core tablet hardly affected drug release in the range of (1.00–1.14) mm. The optimal osmotic tablet was found to be able to deliver atenolol at an approximately constant rate up to 24 h, independent of both release media and agitation rate.\textsuperscript{28}

**Lu et al.** prepared a monolithic osmotic tablet system with two orifices in both side surfaces. Water-insoluble naproxen was selected as the model drug. Gum arabic was used as an osmotic, suspending and expanding agent and cellulose acetate (CA) was used as semipermeable membrane. Polyethylene glycol 400 (PEG-400) was employed as plasticizer for controlling membrane porosity. The influences of gum arabic, PEG-400, membrane thickness and orifice size on the naproxen release profiles were investigated, and the optimal monolithic osmotic tablet was evaluated in different environment media and stirring rates. The optimal monolithic osmotic tablet was found to be able to deliver naproxen at a rate of approximately zero order up to 12 h in pH 6.8, cumulative release at 12 h is 81\%, independent on environment media and stirring rate. Therefore, this monolithic osmotic tablet can be used in oral drug controlled delivery field, especially for water-insoluble drug.\textsuperscript{29}

**Li et al.** developed a controlled release effervescent osmotic pump tablet of Traditional Chinese Medicine Compound Recipe (TCMCR), named Fuzilizhong prescription which includes acidic drugs consisted of many known and unknown effective components and has been used for several thousands years, was successfully prepared with sodium chloride, sodium hydrogen carbonate and hydroxyl propyl methyl cellulose (HPMC) as osmotic agents. Since the osmotic pressure in osmotic tablet with sodium chloride and sodium hydrogen carbonate increased greatly, this was induced mostly by gas carbon dioxide generating from the reaction of sodium hydrogen carbonate and the acidic drugs in TCMCR after the fluid being imbibed into the compartment through the semipermeable membrane. The problem that water insoluble drugs can not to be elementary osmotic pump tablet for its low dissolution rate was solved in the paper. The drug in effervescent osmotic pump tablet was released controllably after HPMC was
selected as retarder and has a good in-vitro–in-vivo correlation (IVIVC, r = 0.9550). Therefore, it could be concluded that the formulation of TCMCR is appropriate to being made into effervescent osmotic pump, which improves acidic drugs composed of soluble and poorly soluble components release more greatly and controllably. From the point of this, water insoluble drugs can be designed to elementary osmotic pump tablet for more complete dissolution release.\textsuperscript{30}

**Tarvainen et al.** prepared aqueous starch acetate dispersion as a novel coating material for controlled release products. The aim of that study was to evaluate film-formation properties of a novel, organic solvent-free aqueous dispersion of potato starch acetate and its ability to control drug release from a coated tablet. Initially, film-formation mechanisms and drug permeabilities of both organic solvent and dispersion-based starch acetate free films (prepared by cast or spraying techniques) were investigated. The starch acetate dispersion was suitable for the fluid-bed coating process, forming strong films with complete coalescent polymeric spheres. The model compounds predominantly permeated via the micro-pores of starch acetate free films, which resulted from the leaching of water-soluble excipients from the dispersion. Thus, the permeation rate depended on the film structure rather than the physico-chemical properties of the penetrant. In the case of starch acetate coated tablet, drug release was sustained when the coating level was increased (from 12\% to 20\%, stated as a weight gain), and also as lipophilicity of the drug increased. When compared to the reference polymer dispersion (Surelease\textsuperscript{R}), starch acetate coatings showed better mechanical properties against the osmotic pressure caused by a hydrophilic core tablet. These results clearly demonstrate that starch acetate dispersion has high utility as a novel aqueous coating material for controlled release products.\textsuperscript{31}

**Sastry and coworkers** formulated osmotically controlled drug delivery systems of atenolol. Preparation involved the fabrication of biconvex, bilayered tablets containing drug, an osmotic agent and other additives. For formulation optimization, a three-factor, three level Box-Behnken design was employed with independent variables of orifice size (X1), coating level (X2), and the amount of Carbopol 934 (X3). The response variable
was cumulative percent of atenolol released with constraints on time for 10, 25, 50 and 75% release. Preparation and testing of the optimized formulation showed a good correlation between predicted and observed values.  

Verma and Garg developed and evaluated extended release formulation of glipizide based on osmotic technology. The effect of different formulation variables, namely, level of solubility modifier in the core, membrane weight gain, and level of pore former in the membrane, were studied. Drug release was found to be affected by the level of solubility modifier in the core formulation. Glipizide release was inversely proportional to the membrane weight but directly related to the initial level of pore former (PVP) in the membrane. Burst strength of the exhausted shells increased with the weight gain of the membrane. On the other hand, burst strength decreased with an increase in the level of pore former in the membrane. Drug release from the developed formulations was independent of pH and agitational intensity, but dependent on the osmotic pressure of the release media. Results of SEM studies showed the formation of pores in the membrane from where the drug release occurred. The numbers of pores were directly proportional to the initial level of pore former in the membrane. The manufacturing procedure was found to be reproducible and formulations were stable after 3 months of accelerated stability studies.  

Tuntikulwattana et al. studied the influence of hydrogel on drug release from microporous osmotic pump tablets. To create the microporous for osmotic pump tablets, a water soluble substance or hydrogel is added to the semipermeable film former solution. In that study, propranolol tablets were prepared and coated with cellulose acetate containing povidone (PVP) as hydrogel. The drug dissolved from core tablet at 1 hr was 80%. The tablets were coated with 3% w/v cellulose acetate in acetone and isopropyl alcohol solution containing PVP K30 or PVP K90 at concentrations of 12.5%, 25% and 50% by weight with respect to cellulose acetate. The coated tablets exhibited the increases in weight and hardness, and decrease in friability. The drug dissolution increased with the PVP concentrations. Without PVP the drug release at 12 hr was 28.5%. With the addition of 12.5%, 25%, and 50% PVP K30, the percent releases were
55.6, 79.9, and 87.2, respectively. With 12.5% and 25% PVP K90, the percent releases were 73.2 and 86.8, respectively. At a given PVP concentration, PVP K90 gave higher dissolution than did PVP K30. Both amount and type of PVP affected the release of propranolol from the tablets.\textsuperscript{34}

\textbf{Liu et al.} formulated chitosan-based controlled porosity osmotic pump for colon-specific delivery system. A microbially triggered colon-targeted osmotic pump has been studied. The gelable property at acid condition and colon-specific biodegradation of chitosan were used to: (1) produce the osmotic pressure, (2) form the drug suspension and (3) form the in situ delivery pores for colon-specific drug release, respectively. The scanning electron microscopy (SEM) study and the calculation of membrane permeability were applied to elucidate the mechanism of microbially triggered colon-targeted osmotic pump. The effects of different formulation variables, including the level of pH-regulating excipient (citric acid) and the amount of chitosan in the core, the weight gain of semipermeable membrane and enteric-coating membrane, and the level of pore former (chitosan) in the semipermeable membrane, have been studied. Results of SEM showed that the in situ delivery pores could be formed in predeterminated time after coming into contact with dissolution medium, and the number of pore was dependent on the initial level of pore former in the membrane. The amount of budesonide release was directly proportional to the initial level of pore former, but inversely related to the weight of semipermeable membrane. The effects of variations in the level of citric acid and chitosan in the core formulation on drug release were studied. The different levels of enteric-coating membrane could prevent cellulose acetate membrane (containing chitosan as pore former) from forming pore or rupture before contact with simulated colonic fluid, but had no effect on the drug release. Budesonide release from the developed formulation was inversely proportional to the osmotic pressure of the release medium, confirming that osmotic pumping was the major mechanism of drug release. These results showed that microbially triggered colon-targeted osmotic pump based on osmotic technology and microbially triggered mechanism had a high potential for colon-specific drug delivery.\textsuperscript{35}
Philip and Pathak developed and evaluated a nondisintegrating, controlled release, asymmetric membrane capsular system of flurbiprofen for controlled release of the drug to overcome some of its side effects. Asymmetric membrane capsules were prepared using fabricated glass mold pins by phase inversion process. The effect of different formulation variables was studied based on $2^3$ factorial design; namely, level of osmogen, membrane thickness, and level of pore former. Effects of polymer diffusibility and varying osmotic pressure on drug release were also studied. Membrane characterization by scanning electron microscopy showed an outer dense region with less pores and an inner porous region for the prepared asymmetric membrane. Differential scanning calorimetry studies showed no incompatibility between the drug and the excipients used in the study. In vitro release studies for all the prepared formulations were done ($n = 6$). Statistical test (Dunnett multiple comparison test) was applied for in vitro drug release at $P > .05$. The best formulation closely corresponded to the extra design checkpoint formulation by a similarity ($f_2$) value of 92.94. The drug release was independent of pH but dependent on the osmotic pressure of the dissolution medium. The release kinetics followed the Higuchi model and the mechanism of release was Fickian diffusion.

Rani and Mishra done comparative in vitro and in vivo evaluation of matrix, osmotic matrix, and osmotic pump tablets for controlled delivery of diclofenac sodium. All formulations were evaluated for various physical parameters, and in vitro studies were performed on USP 24 dissolution apparatus II in pH 7.4 buffer and distilled water. In vivo studies were performed in 6 healthy human volunteers; the drug was assayed in plasma using HPLC, and results were compared with the performance of 2 commercial tablets of diclofenac sodium. Various pharmacokinetic parameters (i.e., Cmax, Tmax, area under the curve and mean residence time) and relative bioavailability were compared. All fabricated formulations showed more prolonged and controlled diclofenac sodium release compared with commercial tablets studied. The osmotic matrix and osmotic pump tablets, however, performed better than the matrix tablets. Type of porosigenic agents and osmogens also influenced the drug release. Analysis of in vitro data by regression coefficient analysis revealed zero-order release kinetics for osmotic matrix and osmotic pump tablets, while matrix tablets exhibited Higuchi kinetics. In vivo results indicated
prolonged blood levels with delayed peak and improved bioavailability for fabricated tablets compared to commercial tablets. It was concluded that the osmotic matrix and osmotic pump tablets could provide more prolonged, controlled, and gastrointestinal environmental independent diclofenac sodium release that may result in an improved therapeutic efficacy and patient compliance. 

Jonnalagadda and Robinson designed and characterized a zero-order bioresorbable reservoir delivery system (BRDS) for diffusional or osmotically controlled delivery of model drugs including macromolecules. The BRDS was manufactured by casting hollow cylindrical poly (lactic acid) (PLA): polyethylene glycol (PEG) membranes (10 x 1.6 mm) on a stainless steel mold. Physical properties of the PLA: PEG membranes were characterized by solid-state thermal analysis. After filling with drug 5-fluorouracil [5FU] or fluorescein isothiocyanate - dextran:mannitol, 5:95 wt/wt mixture) and sealing with viscous PLA solution, cumulative in vitro dissolution studies were performed and drug release monitored by ultraviolet (UV) or florescence spectroscopy. In vitro release studies demonstrated zero-order release of 5FU for up to 6 weeks from BRDS manufactured with 50% wt/wt PEG. The release of FITC dextran of molecular weights 4400, 42000, 148000, and 464000 followed zero-order kinetics that were independent of the dextran molecular weight.

Mishra and coworkers formulated oral push-pull osmotic pumps of pentazocine hydrochloride. Push-Pull osmotic pumps of pentazocine HCl were prepared using different formulation variables like diameter of pores, presence of surfactant in formulation core, addition of osmopolymer pectin and presence/absence of water-soluble polymer (carboxymethylcellulose sodium). Fabricated osmotic pumps were evaluated for weight variation, coating thickness, pore diameter, drug content and in vitro release studies. Release rates were found to be independent of size of pores, agitation intensity, and pH of the release medium. The presence of surfactant, water-soluble polymer and osmopolymer (pectin) affected the drug release significantly. Almost all the osmotic pumps gave controlled and prolonged drug release profiles beyond 2 h of lag phase.
**Wang et al.** developed asymmetric membrane capsules for delivery of poorly watersoluble drugs by osmotic effects. A non-disintegrating polymeric capsule system, in which asymmetric membrane offers an improved osmotic effect, was used to deliver poorly water-soluble drugs in a control manner. The capsule wall membrane was made by a phase inversion process, in which asymmetric membrane was formed on stainless-steel mold pins by dipping the mold pins into a coating solution containing a polymeric material followed by dipping into a quench solution. This study evaluates the influence of coating formulation that was cellulose acetate, ethylcellulose, and plasticizer (glycerin and triethyl citrate). Results show capsule that made by cellulose acetate with glycerin, which appear in asymmetric structure and are able to release chlorpheniramine maleate in significant percentage. Two poorly water-soluble drugs of felodipine and nifedipine were selected as the model drug to demonstrate how the controlled release characteristics can be manipulated by the design of polymeric capsules with an asymmetric membrane and core formulations. Results show that sodium lauryl sulfate (SLS) is able to promote the release of felodipine from polymeric capsules prepared with cellulose acetate with asymmetrical membrane. The addition of solubilizer, including RH40, PVP K-17, and PEG 4000 could enhance the release of felodipine but with an extent not being related to its solubility. Based on these results, influence of core formulation variables, including the viscosity and added amount of hydroxyl propyl methyl cellulose (HPMC), the added amount of SLS, and drug loading were examined on the release of nifedipine. It was found that HPMC of 50 cps was suitable to be a thickening agent and both added amount of HPMC and SLS showed a comparable and profoundly positive effect, whereas nifedipine loading had no influence on the drug release percent and rate. There existed a synergistic interaction between HPMC and SLS on the release percent and rate.40

**Liu et al.** formulated the monolithic osmotic tablet system, which is composed of a monolithic tablet coated with cellulose acetate membrane drilled with two orifices on both side surfaces, has been described. The influences of tablet formulation variables including molecular weight (MW) and amount of polyethylene oxide, amount of potassium chloride (KCl), and amount of rice starch as well as nifedipine loading have been investigated. Orifice size and membrane variables including nature and amount of
plasticizers as well as thickness on drug release have also been studied. The in vitro release profiles of the optimal system have been evaluated in various release media and different agitation rates, and compared with commercialized conventional capsule and push–pull osmotic tablet. It was found that polyethylene oxide with MW of 300 000 g/mol was suitable to be thickening agent, both amount of KCl and amount of polyethylene oxide had comparable and profoundly positive effects, while nifedipine loading had a strikingly negative influence on drug release. It could be found that the optimal orifice size was in the range of 0.25–1.41 mm. It has also been observed that hydrophilic plasticizer polyethylene glycol (PEG) improved drug release, whereas hydrophobic plasticizer triacetin depressed drug release when they were incorporated in cellulose acetate membrane. The monolithic osmotic tablet system was found to be able to deliver nifedipine at the rate of approximate zero-order up to 24 h, independent of both environmental media and agitation rate, and substantially comparable with the push–pull osmotic tablet. The monolithic osmotic tablet system was simple to be prepared as exempting from push layer and simplifying in the orifice drilling compared with the push–pull osmotic tablet. The monolithic osmotic tablet system may be used in drug controlled delivery field, especially suitable for water-insoluble drugs.\textsuperscript{41}

\textbf{Thombre et al.} studied osmotic drug delivery using swellable-core technology. Swellable-core technology (SCT) formulations that used osmotic pressure and polymer swelling to deliver drugs to the GI tract in a reliable and reproducible manner were studied. The SCT formulations consisted of a core tablet containing the drug and a water-swellable component, and one or more delivery ports. The in vitro and in vivo performance of two model drugs, tenidap and sildenafil, formulated in four different SCT core configurations: homogeneous-core (single layer), tablet-in-tablet (TNT), bilayer, and trilayer core, were evaluated. In vitro dissolution studies showed that the drug-release rate was relatively independent of the core configuration but the extent of release was somewhat lower for the homogeneous-core formulation, particularly under non-sink conditions. The drug-release rate was slower with increasing coating thickness and decreasing coating permeability, and was relatively independent of the drug loading and the number and size of the delivery ports. The drug-release rates were similar for the two
model drugs despite significant differences in their physicochemical properties. Tablet-recovery and pharmacokinetic studies conducted in beagle dogs showed that the in vivo release of drug from SCT formulations was comparable to the in vitro drug release.\textsuperscript{42}