EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 4
121-126
Year: 2022

A REVIEW ON OSMOTIC DRUG DELIVERY SYSTEM

Pallavi Sonkar[1]* and Vivek Kumar Patel[2]

Research Scholar, SHEAT College of Pharmacy, Varanasi.
[2]Assistant Professor, SHEAT College of Pharmacy, Varanasi.

***Corresponding Author: Pallavi Sonkar**
Research Scholar, Krishna Puri Colony, Varanasi.

Article Received on 24/01/2022 **Article Revised on 14/02/2022** **Article Accepted on 04/03/2022**

ABSTRACT
Conventional drug has little control over their drug release and almost no control over the effective concentration at the target site. This type of dosing pattern may result in fluctuation in plasma concentration. Hence to avoid the shut comings there is development of various osmotic drug delivery system (ODDS). The ODDS utilizes the basic principle of osmotic pressure for controlled release of drug and it delivers drug in optimized manner to maintain drug concentration within their therapeutic window & minimize side effect. The release of drug from osmotic system depends upon various formulation factor such as solubility, osmotic pressure of core components, size of delivery orifice and nature of rate controlling membrane. This review paper highlights the theoretical concepts of drug delivery, principle and types of osmotic drug delivery system with basic component has been discussed briefly.

KEYWORDS: Osmosis, Osmotic Drug Delivery System, Osmotic Pressure, Controlled Formulation, Osmotic Pump.

1. INTRODUCTION

Oral route is the most preferred and convenient choice as the oral route provides maximum active surface area among all drug delivery system for administration of various drugs.[1] In conventional oral drug delivery systems there is little or no control ever release of the drug and effective concentration at the target site can be achieved by irregular administration of excessive doses. The rate and extent of drug absorption from conventional formulation charge significantly depending on factors such as presence of recipients, physicochemical properties of the drug, various physiological factors such as presence of or absence of food, P^H of gastro intestinal and so on.[2] To overcome these shortcomings researchers have focused on the development of Osmotically controlled drug delivery systems (OCDDS) is the most promising drug delivery technology that use osmotic pressure as a driving force for controlled delivery of active agents. Drug release from OCDDS is independent of P^H and hydrodynamic condition of the body because of the semi-permeable nature of the body because of the semi-permeable nature of the rate-controlling membrane and the design of delivery orifice used in osmotic systems, so a high degree of inviter correlation is achieved.[3] Osmosis refers to process movement of solvent from lower concentration of solute towards higher concentration of solute across a semi permeable membrane. Osmotic pressure is minimum pressure which needs to be applied to a solution to prevent the inward flow of its pure sonnet across a semiperme membrane as drug delivery system.

Now days, Osmotic tablets have been the delivery orifice is formed by the incorporation of a liable component in the coating. Once the tablet comes in contact with the aqueous environment, the water soluble component dissolves and an osmotic pumping system result. Subsequently, water diffuses into the core through the micro porous membrane, setting up an osmotic gradient and thereby controlling the release of drug.[4] Controlled drug release systems attempts to sustain drug action at a predetermined rate by maintain a relatively constant, effective drug level in the body with minimization of undeniable side effects.

In oral NDDS (Novel Drug Delivery System) the development of the Osmotic Drug Delivery System is a significant milestone by an innovative and highly versatile drug delivery system. Osmotic Drug Delivery System (ODDS) differ from diffusion based system in that; the delivery of the active agent(s) is driven by an osmotic gradient rather them the concentration of drug in the dare [Ends et al-2005]. Osmotic devices are most promising strategy based systems for controlled drug delivery. These drug delivery are unique in the sense that the delivery drug(s) is not dependent/influenced by physiological variables within the GITC Gastro intestinal tract), these systems are adaptable to a number of drugs, with minor modulation and the delivery of drug(s) can be made. They are also known as GITS (gastro-intestinal and now, different types of osmotic pumps, of various drugs, are available in the market to meet patients need and requirement.[5]

2. Advantages

- Drug release from osmotic pump is independent of the gastric pH and hydrodymic condition of the body.
- Higher releases rates are possible in Osmotic systems rather than with conventional diffusion based drug delivery system.
- Having easy formulation and simple operation.
- The delivery rate of drug(s) from these systems is highly predictable and programmable by modulating the release control parameters.
- Improved patient compliance with reduced dosing frequency.
- It is having better release rates than those obtained with conventional diffusion.
- Enhanced bioavailability of drug.
- Reduced side effects.
- Increased safety margin of high potency drugs.
- Delivery may be delayed or pulsed, of desired.
- They are suitable for a wide range of drug.
- Sustained and consistent blood levels within the therapeutic window.
- They are well charactered and understood.
- Reduced interpatient variability.

3. Disadvantage

- High Court.
- It the coating process is not well controlled there is a risk of film defects, which results in dose dumping.
- Hole size is critical in case of elementary osmotic system.
- Drug release from the osmotic systems is affected it some extent by the presence of food.
- Retrieval of therapy is not possible in the case of unexpected adverse event.
- Rapid development of tolerance.[6]

4. Principle and Basic concept of osmotic drug delivery system

It is based on the principle of osmotic pressure. Osmotic pressure is dependent on concentration of solute which contributes to osmotic pressure solutions of different concentrations having the same solvent and solute system that show an osmotic pressure proportionate to their concentrations. Thus a constant osmotic pressure and thereby a constant influx of water can be achieved by an osmotic drug delivery system. Which results a constant zero order release rate of drug. The rate of drug release from osmotic pumps depends on osmotic pressure of the core and the drug solubility; hence, these systems are suitable for delivery of drugs with moderate water solubility.[7]

Abbe Nollet was the first person to report the osmotic phenomena in 1748; but prefer seperate sugar solution from pure water by using selectively permeable membrane. Here, osmotic pressure is proportionate to temperature and concentration. Further, Vant Hoff in 1886 express this proportionality in the form of a equation which is as follows:

$\pi = n2\ RT$

where, π = osmotic coefficient

n2 = molar concentration of solute in the solution

R = gas constant

T = Absolute temperature.[8]

5. Basic components of osmotic pump

5.1 Drug

Drug which have short biological half-life (2-6 hrs), highly potent and which is used for prolonged treatment are ideal for osmotic systems. There are various drug such as Diltiazen HU, carbamazeptne, Metoprolol, Nifedipine, Glipizide, verapamil, losartan etc. are formulated as Osmotic delivery (Sharma S. 2008).

5.2 Oxmotic Components/Osmogents

Osmotic agents are essential ingredient of the osmotic formulation. Osmotic components usually are ionic compounds consisting of either inorganic salts hydrophilic polymers or carbohydrates. Different type of osmogents can be used for such systems are categorized as water soluble salts of inorganic acids like magnesium chloride or sulphate; lithium, sodium or potassium chloride; sodium or potassium hydrogen phosphate water-soluble salts of organic acids like sodium and potassium acetate, magnesium succirate, sodium literate; Carbohydrate like mannese, sucrose, matter lactose; water- solukle (amino acid) and organic polymeric osmogents, etc (Gaduat et al, 2010).

Polymeric osmogents are nvoty used in the fabrication of osmatically controlled drug delivery systems and other modified dates for controlled release of relatively insoluble drugs.[9]

5.3 Simipermeable Membrane (SPM)

Semipermeable mebrane is also known as selectively permeable membrane or partially permeabel membrane or differentially permeable membrane. Anything or material that permits water but does not permit solute passage through it can be used as this membrane. Semipermeable membrane shoudl be a stable both to the cuter and inner environment of device. The membrane must be adequate unbending in order to held its dimensional uprightness during the operational lifetime of the device. The membrane must be biocompatible. e.g. cellulose acetate, agar acetate, amylesetriacetate, beta gluc an acetate etc.[10]

5.4 Coating Solvents

There are various solvent suitable for making polymeric solution that is used for manufacturing the wall of the osmotic device utrich includes input inorganic and organic sowents.

E.g. methfene chloride, acetone, methanel, ethanel, isopropyl alcohol, ethyl acetate, cycloherane etc.[11]

5.5 Emulsifying agent/Surfactant

Emulsifying agent are particularly useful when coded to wall forming material they produce an integral composite that is useful for making the wall of the device operative the emulsifying agent act by regulating the surface energy of material to improve their blending in to the composite and maintain their integrity in the environment of use during the drug release period. Typical surfactants such as poly oxyethyenated glyceryl recinoleoate, polyoxythlenated, castor oil having ethylene oxide, glyceryl locureates, glycerol etc.

5.6 Flux regulators

Flux regulating agents or flux enhancing agent or flux decreasing agent are added to a wall forming material it assists in regulating the fluid permeability through membrane. The flux regulating agent may be hydrophilic substances and hydrophobic substances. The hydrophilic substances such as polyethylene glycols, polyhydric alcohols, polyalkylene glycols increase the flux whereas hydrophobic substances such as phthalates substituted with alkyl or alkoxy (diethyl pththalates dimethgloxyethyl phthalate) decrease flux.[12]

5.7 Wicking agents

It is defined as the agent which is required to bring the water inside the device, which enhance contact of water with the device. The function of wicking agent to or to attract carry water to surface inside the center of tablet, thereby making channels or network to increased surface area. They can be sellable or non-sellable. Examples of wicking agent are colleidal silicon dioxide, Kaolin, litanium dioxide, Sodium lauryl, sulphate (SLS), alumina, niacinamide, polyvinyl pyrrolidone (PUP) etc.'

5.8 Plasticizers

Plasticizer lower the temperature of the second order phase transition of the elastic modules of the wall and also increase the workability, flexibility and permeability of the fluids generally from 0.001-50 parts plasticizer or admixture of plasticizers are incorporated into 100 parts of wall forming materials. E.g. dialky Phthalates and phth alates, trioctyl phosphates, benzoates, sulphanamides, glyceuolates.[13]

5.9 Pore forming agent

Drug which are not soluble in water these materials are used which are inorganic, organic, solid or liquid in nature. The pore forming agent form microporous structure in the membrane due their leaching during the operation of the system. The pores may also be formed in the wall prior to operation of the system. By gas formation within coating polymer solutions which result in void and pore in the final form of wall. E.g. Alleatine metal salts such as sodium chloride, sodium bromide, potassium Chloride, potassium sulphate etc. alkaline earth metals like calcium chloride and calcium nitrate. Carbohydrates like source, glucose, fructose, mannose, sorbitol and manitols, diols, polyols etc.[14]

5.10 Hydrophillic and Hydrophebic polymers

Used in the formulation development of osmotic systems containing drug matrix core. The selection of polymer is based on solubility of the drug or amount and rate of drug to be released from the device. Exmaple of hydrophillic polymers- HEI (Hydroxyl Ethyl Cellulose), HPMC (Hydroxyl Proply Methyl Cellulose) and example of hydrophobic polymers- EC (Ethyl cellulose, wax materials etc.).[15]

6. Types of osmotic drug delivery systems (Sharma S. 2008)

6.1 Single Chamber Osmotic System:
6.1.1 Elementary Osmotic Pump.
6.2 Multi chambered Osmotic System.
6.2.1 Push-pull Osmotic Pumps.
6.2.2 Sandwiched Osmotic Pump.
6.2.3 Osmotic Pump with non-expanding Second Chamber.
6.3 Specific Types.
6.3.1 Controlled-Porosity Osmotic Pumps.
6.3.2 Monolithic Osmotic Pump Tablet.
6.3.3 Colon targeted Oral Osmotic System (Oros T).
6.3.4 Osmotically Brusting Osmotic Pump.
6.3.5 Asymmetrical Membrane Osmotic Tablet.
6.3.6 Liquid Oral Osmotic System.
6.3.7 Effervescent Osmotic pump tablet.
6.3.8 Multiparticulate Delayed-Release System (osmotic pellet)
6.3.9 Self Emulsified Osmotic Tablet.
6.3.10 Telescopic Capsule for Delayed-Release[16]

6.1.1 Elementary osmotic pump

The elementary Osmotic pump is a new delivery system for drugs which delivers the drug by an osmotic process at a controlled rate. This system contains osmotically active agent surrounded by the rate controlling semipermeable membrane. The device is formed by compressing a drug having a suitable osmotic pressure into a tablet-using tableting machine.[17]

When the dosage form exposed to the aqueous environment, the core imbibes water osmotically at a controlled rate, which is determined by the water permeability of the semipermeable membrane and the osmotic pressure of core formulation. The volume of saturated drug solution delivered is equal to the volume of solvent uptake. This increases the hydrostatic pressure inside the tablet forces the saturated drug solution through the hole present in film. These systems are suitable for delivery of drug having moderate water solubility.[18]

6.2 Multi chambered osmotic system

6.2.1 Pull-push Osmotic Pumps (PPOP)

It is a bilayered tablet which is coated with semipermeable membrane. Drug osmogent is present in the upper section 60-80% & lower section consists of polymeric osmotic agent at 20-40% when dosage form come in contact with aqueous environment, both compartments imbibe water simultaneously because lower compartment is avoid of any orifice, it expands and pushes the diaphragm into upper drug chamber, there by delivering the drug via the drug orifices. These systems deliver both highly water soluble and practically insoluble.[19]

6.2.3 Osmotic pump with non-expanding second chamber

The second category of multi-chamber devices comprises system containing a non-expanding second chamber. The purpose of second chamber is either dilution of drug solution leaving the device (particularly useful in handling drugs with high incidence of GI irritation) or simultaneous delivery of two drugs. Relatively insoluble drug can also be delivered.[20]

6.3 Specific types

6.3.1 Controlled-porosity Osmotic Pumps (CPOP)

CPOPs are similar to EOP, the only difference being that the delivery orifice from which the drug release take place is formed by incorporation of a water soluble additive in the coating. It is an osmotic device device wherein the delivery orifices are formed in site through leaching of water soluble pore-forming agents incorporated in semipermeable membrane. Drug release rate from controlled porosity osmotic pump depends on various factors like coating thickness, level of leachable pore-forming agent(s) solubility of drug in tablet core, and the osmotic pressure difference across the membrane. The stomach irritation problems are significantly reduced, as drug is released from the whole of the device surface rather from a single hole. Further, no complicated laser-drilling unit is required because the delivery orifices are formed in site.

6.3.2 Monolithic Osmotic Pump Tablet (MOP)

The monolithic osmotic system consists of a simple disperson of water-soluble agent in a polymer matrix. When MOS comes in contact with the aqueous environment, the water imbibitions by the active agent takes place rupturing the polymer matrix capsule surrounding the drug, thus liberating drug to the outside environment. Initially this process occurs at the matrix in a serial fashion. However this system fails if more than 20-30 volumes per liter of the active agents are incorporated in to the device as above this level, significant contribution from the simple leaching of the substance take place.[21]

6.3.3 Colon Targeted Oral Osmotic System (Oros CT)

This system can be used for once or twice a day formulation for targeted delivery of drugs to the colon. The system is coated with 5-6 enteric coating and push-pull osmotic units filled in hard gelatin capsule for targeted colonic drug delivery.[22] When gelatin capsule shell dissolves after coming in contact with GI fluids, the entry of fluid from stomach is inhibited by outer shell of the system and it dissolves after entering into intestine. The water imbibes into the core and push compartment will swell. At the same time, the flow able get is formed which is pushed out via delivery orifice at predetermined rate.[23]

6.3.4 Osmotically brusting osmotic pump

In this system delivery orifice is absent and size of orifice is small than elementary osmotic system (EOP). When it is placed in aqueous environment, water is imbibed and hydraulic pressure is built up inside until the wall rupture and the contents are released to the environment. Varying the thickness as well as the area the semipermeable membrane can control release of drug. This system is useful to provide pulsated release.[24]

6.3.5 Asymmetrical membrane osmotic tablet

Asymmetric membrane capsules consist of a drug containing core surrounded by a membrane which has an asymmetric structure; it has relatively thin, dense region supported on a thicker, porous region. The capsule wall is made from a water insoluble polymer such as cellulose acetate unlike a conventional gelatin capsule; the asymmetric membrane capsule does not dissolve immediately but provides prolonged release of the active ingredient in corporate in the capsule.[25]

6.3.6 Liquid Oral Osmotic System (L-OROS)

Liquid OROS are designed to deliver drugs as liquid formulations and combine the benefits of extended release with high bioavailability. These systems are suitable for controlled delivery of liquid drug formulation including lipophillic self-emulsifying formulation (SFF). They are two types-

(a) Liquid OROS soft cap.
(b) Liquid OROS hard cap.

(a) Liquid OROS Soft Cap

In soft cap, liquid drug formulations present in a soft gelatin capsule, which is surrounded with the barrier layer osmotic layer and the release rate-controlling membrane.

(b) Liquid OROS Hard Cup

In hard cap, it consists of a liquid drug layer and an osmotic engine, all encased in a hard gelatin capsule and coated with semi-permeable membrane. The expansion of the osmotic layer results in the development of hydrostatic pressure inside the system, thereby forcing the liquid formulation to the delivered from the delivery orifice. This technology allows the delivery of insoluble drugs in aqueous fluids and is reported to increase the permeability of the drugs.[26]

6.3.7 Effervescent osmotic pump tablet

In this system, effervescent compound are incorporated into dosage form which react with acid in the outer environment produce the carbon dioxide. This gas expands and dispenses the precipitate drug and prevents the blockage of orifice. This system beneficial for poorly soluble drug al low pH may precipitate at the gastric pH and block the delivery orifice. Sodium bicarbonate is usually use in the system.[27]

6.3.8 Multi-particulate Delayed-Release System (Osmotic Pellet)

In this system, pellets containing pure drug with or without osmotic agent are coated with a semipermeable membrane. When this system comes in contact with aqueous environment, water penetrates into the core and forms a saturated solution of soluble components. The osmotic pressure gradient includes a water influx, leading to rapid expansion of the membrane and formation of the pores. The release of osmotic ingredient(s) and the drug through these pores tend to follow zero-order kinetics.[28]

6.3.9 Self emulsified osmotic tablet

In this case of slightly soluble or practically insoluble drugs, self-emulsifying agents have been added to the tablet-core composition. Self emulsifying system improves the bio-availability of drug, controlled release rate and make the plasma concentrations more stable by self-emulsifying agent. It emulsifies the hydrophobic drugs. There are various surfactants such as poly oxyethylenated glyceryl recinoleate, custore oil such such as ethylene oxide, glyceryl laureates, glycerol etc. have been used to serve the purpose.[29]

6.3.10 Telescopic capsule for delayed release

This device consists of two chambers, the first contains the drug and an exit part, and the second contains an osmotic engine, a layer of wax like-material separates the two sections.[30] As the fluid imbibed the housing of dispensing device, the osmotic engine expands and exerts pressure on the skiable connected first and second wall section. During the delay period, volume of reservoir containing the active agent is kept constant, therefore a negligible pressure gradient exists between the environment of use and interior of the reservoir. As a result, the net flow of environmental fluid driven by the pressure enter the reservoir is minimal.[31]

7. Market study

In the market, there are thirty- one product has been developed and marketed based on osmotic Drug Delivery System (ODDS) technology. All these products are under the therapeutic areas: cardio vascular (35%), neurological (25%), seasonal (25%) and metabolic disorders (15%). These products have been mainly developed by two companies, the former Alzo Corp, which was later acquired by Johnson & Johnson developed 20 products (53%) and osmotic Pharmaceutical Corp., which was spin-off company of Phoenix Inc., with 10 products (26%).

8. CONCLUSION

Osmotic drug delivery system can be a promising tool in oral drug delivery. Controlled porosity osmotic can be used for designing various formulations containing the osmotic agent, pore former and rate controlling membrane. Optimization of these parameters can control the release of drug as per the time period require. By using this technique the release may be pulsed for the specific in chromo therapy.

ACKNOWLEDGEMENT

I am thankful to the management of institute. All authors listed have significantly contributed to the development and All authors listed have significantly contributed to the development and the writing of this article.

Conflict of interest.

The authors declare no conflict of interest.

REFERENCES

1. Ratnaparkhi, M.P. & Gupta, J.P. Sustained release Oral Drug Delivery System- An Overview International Journal of Pharm Research and Review, 2013; 2(3): 11-21.
2. Khatri Neetu, Nikam Sarika, Bilandi Ajay; Oral Osmotic Drug Delivery System: A Review; International Journal of Pharmaceutical Sciences and Research, 2016; 7(6): 2302-2312.
3. Sahoo Keshari Chimmaya Sahoo Kanta Nalini, Rao Mohan Ram Surepalli Muvvala Sudhakar, Satyanarayna; A Review on Controlled Porosity Osmotic Pump Tablets and its evaluation; Bulletin of faculty of Pharmacy, cairo University, 2015; 53: 195-205.
4. Dhage C.M., Shinkar D.M., Pathan V.T., Jadhav A.G.: A Review on Osmotic Drug Delivery System; International Journal of Pharmaceutical Sciences Review and Research, 2020; 62(1): 160-167.
5. Syed Mohammad Shoaeb, Z. Farooqui, M. Mohammad, Dureshahwar K., M. Farooqui; Osmotic Drug Delivery System: An Overview; International Journal of Pharmaceutical Research & Allied Sciences, 2015; 4(3): 10-20.
6. Ali Nayab; Review Article on Osmotic Drug Delivery System; Research Gat, 2021; 1-19.
7. Lu. xu, sanming s, L., Hisakazu, s.2006, preparation and evaluation invitro and invivo of captopril elementary osmotic pump tablets; asian journal of pharmaceutical sciences, (3-4); 236-245.
8. Gadwall, p.rudrawal, p.ahmed, d. ahmed, 2010, a review on osmoyically regulated devices international journal of pharmacy $ life sciences, 1(6): 302-312.
9. N, Gupta & Rakesh, Gupta & Basniwal, Pawan & S, Rathore. (2010). Osmotically Controlled Oral Drug Delivery Systems: A Review. International Journal of Pharmaceutical Sciences.

10. Bieck, Peter. (1993). Colonic Drug Absorption and Metabolism.
11. Razaghi AM, Schwartz JB. Release of cyclobenzaprine hydrochloride from osmotically rupturable tablets. Drug Dev Ind Pharm. 2002 Jul; 28(6): 695-701. doi: 10.1081/ddc-120003861. PMID: 12149962.
12. Bhanushali, Roopali & Dhurke, Rajeshri & Bajaj, Amrita. (2009). Monolithic Osmotic Tablets for Controlled Delivery of Antihypertensive Drug. Journal of Pharmaceutical Innovation. 4. 63-70. 10.1007/s12247-009-9055-5.
13. Verma RK, Krishna DM, Garg S. Formulation aspects in the development of osmotically controlled oral drug delivery systems. J Control Release. 2002 Feb 19;79(1-3):7-27. doi: 10.1016/s0168-3659(01)00550-8. PMID: 11853915.
14. Li XD, Pan WS, Nie SF, Wu LJ. Studies on controlled release effervescent osmotic pump tablets from Traditional Chinese Medicine Compound Recipe. J Control Release. 2004 May 18;96(3):359-67. doi: 10.1016/j.jconrel.2004.01.026. PMID: 15120893.
15. Schultz, P., & Kleinebudde, P. (1997). A new multiparticulate delayed release system.: Part I: Dissolution properties and release mechanism. Journal of Controlled Release, 47, 181-189.
16. Khavare, NB & Dasankoppa, Fatima & N.G.N, Swamy. (2010). A Review on Key Parameters and Components in Designing of Osmotic Controlled Oral Drug Delivery Systems. Indian Journal of Novel Drug Delivery. 2. 122-31.
17. Gohel, Parikh .R.K, Shah. N.Y. Osmotic Drug Delivery: An Update. Pharma info.net. 2009; 7: 2.:47-50.
18. Lachman L. Lieberman A.H., Kaning LJ. The Theory and Practice of industrial pharmacy, Bombay; Indian Varghese Publishing House, 1987; 3: 293-4.
19. Aulton E.A., Pharmeceutics. The sciences of dosage form Design, Churchill Livingstone, London, 2002; 417.
20. Sharma, S. Osmotic Drug Delivery System Pharmainto net, 2008; 6(3).
21. Lu Xu, Sanming, L., Hisakazu, S. Preparation and evaluation in vitro and in vivo of cuptoprilmn elementary osmotic pump tablets; Asian Journal of Pharmaceutical Sciences, 2006; 1(3-4): 236-245.
22. Gadwal, P., Rudrawal, P., Ahamad, D., Ahmed A., A Review on Osmotically Regulated devices. International Journal of Pharmacy & Life Sciences, 2010; 1(6): 302-312.
23. Gupta, R.N., Gupta, R., basniwal, P.K., Rathore G.S. Osmotically Controlled Oral Drug Delivery Systems: A Review, International Journal of Pharmaceutical Sciences, 2009; 1(2): 269-275.
24. Theuwes F., Wong P.S., Burkoth T.L., Fox D.A., R.R. Bicek, "In: Colonic drug absorption and metabolism", Marcel Decker, new York, 1993; 137-158.
25. Amir, M., Joseph, B. Release of Cyclobenzaprine Hydro-chloride from Osmotically Reputable Tablets, Drug Development and Industrial Pharmacy, 2002; 28: 695-701.
26. Bhanushali, R., Rajeshri, W., Amrita, B. Monolithic Osmotic Tablets for Controlled Delivery of Antihy pertensive Drug, Journal of Pharma Innovation, 2009; 4: 63-70.
27. Verma, R.K., Divi, M.K., Garg, S. Formulation aspects in the development of osmotically controlled oral drug delivery systems, Journal of Controlled Release, 2002; 79: 7-27.
28. Xio-dong Lee, Wei-san Pan, Shoe-fan Lee, Li-ju Wu, Studies on controlled release effervescent osmotic pump tablet from traditional Chinese medicine compound recap, Journal of Controlled Release, 2004; 96: 359-367.
29. Schultz, P., kleinebudde, P. A New Multiparticulate delayed release system. Part I: Dissolution properties and release mechanism. Journal of Controlled Release, 1997; 47: 181-189.
30. Khavare, N.B., Fatima, S.D., Najundaswamy, N.G., 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): 122-131.
31. Gohel, M. Parikh, R.K., Shah, N.Y., Osmotic Drug Delivery: An Update Pharmainfo.net, 2009; 7(2): 47-50.