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A REVIEW ON NATURAL POLYMER USED IN ORAL DRUG DELIVERY MATRIX TABLET

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ABSTRACT
For sustained and controlled release of drugs matrix tablet is an most important tool. For administration of drugs oral route is most popular route. For sustained and controlled release of drugs tablets plays an important low cost approach. For water soluble and water insoluble drugs matrix tablets are mostly used for sustained release of drugs. Most widely used polymer in matrix tablet is hydrophilic polymer. In the preparation of matrix tablets, different types of polymers are used for controlling the release of drugs has develop most important tool. From matrix tablet drug release by both Dissolution controlled as well as diffusion controlled mechanism. Released of drugs from polymer matrices by complex interaction between swelling, Diffusion and erosion depending on the nature of the drug. In case of hydrophilic drugs, drug release is mediated mostly by diffusion mechanism.

KEYWORDS: Matrix tablet, Natural polymer, Sustained release, oral route, Patient convenience and compliance.

INTRODUCTION

Oral drug products such as tablets and capsules are most popular solid unit dosage form. Oral drug delivery system is safest route of drug administration to treat various diseases. These are formulated to release the drug (active) immediately after oral administration. These oral dosage forms are formulated for obtaining rapid and systemic drug absorption. Oral drug delivery formulation may vary significantly bioavailability of drug. Bioavailability depend on factors physiocochemical properties of the drug and presence of excipients etc. The drug release can be regulate by different types of methods but the number of novel drug delivery systems are prepared by using matrix reservoir or osmotic principle.

For the pharmaceutical industry, establishing safe and well regulated drug delivery system is one of the big challenges. For this, characteristics of drugs and form in which they are given must be improved. For sustained and controlled release of drugs matrix is most important tool. For administration of drugs oral route is most popular route. For sustained and controlled release of drugs tablets plays an important low cost approach. Most widely used polymer in matrix tablet is hydrophilic polymer. In the preparation of matrix tablets different types of polymers are used for controlling the release of drugs has become most important tool. From the matrix tablet, drug release by both dissolution controlled mechanism as well as diffusion controlled mechanism.

For increasing of patient compliance and therapeutic efficacy, the oral sustained drug delivery system is the most widely used method for giving of therapeutic agents for systemic effect. For prolong and sustain release of drugs, the tablet matrix is formed by the help of hydrophilic and hydrophobic polymers. Now a days we have awareness for the development of matrix sustained release formulations such as matrix tablet containing hydrogels.[4]

Hydrophobic lipid matrix system mostly used in controlled delivery of drug applications due to their chemical inertness, low cost, legal acceptance and compliance of attaining the need release profile of drug. The matrix system of controlled release delivers the drug systemically for a specified duration of time at predetermined rate.[8] The aim of such matrix system is to give sensible delivery profiles that can attain therapeutic plasma levels.

Release of drug is depend on properties of polymer, consequently the application properties of these can build well specified and consistent dosage forms. If the system is lucky in keeping constant level of drug in the target tissue and blood, it is regard as a controlled –release system.

Sustain release involve any drug delivery system that attains release of drug slowly over a prolong duration of time. Controlled release system can affect by physiological process such as ionization, pH, enzymes and motility.

Water soluble matrix systems are widely used for oral controlled delivery of drug as they can reproduce a feasible drug profile and low-cost effective. The prime mechanism of drug on contact with the water –solublemedium to form a gel layer on the surface of the system. Dissolution, Diffusion and erosion is the process by which drug is release.[10-12]

Huge date were acquired over the duration of 25 years to review the continuous development in the field of research of matrix tablets.

Advantage of oral matrix system

This class of delivery of drug has numerous satisfaction over conventional dosage forms, some are given below[13-14] :-

- They are easy and simple to formulate.
- The amount of dose is decreased because released of drug over a longer duration of time. This is crucial to the patient with long-term disease and require a plasma drug concentration inside its therapeutic range like as over night long management of pain in disease patients.
- In case of cracking, There is no danger in dumping of Dose.
- Release of high molecular weight compound is made.
- Harmful effects and dumping of dose due to high concentration of plasma is reduced.
- Patient compliance is improved.
- Superior control in concentration of drug.
- In case of some drugs, Bioavailability is improved.
- Expanding the stability by saving the drug from hydrolysis or in gastrointestinal tract there is changes in derivatives.
- There is decreased in doses, so manufacturing cost –effectiveness is possible.
- Decreased in toxicity as drug absorption is slowly.
- Accepted for both non-biodegradable and degradable system.

Disadvantage of oral controlled release formulations

Similarly like others formulations, it has several disadvantage which are given below[15-16]:-

- There should be must removal of left matrix after the releasing of drug.
- There are various factors like food and rate transit through the gut affect the release rate of drug.
- There cost of preparations is high.
- Difficult to attain zero order release.
- Releasing rate of drug vary with the square root of time.
- High cost equipment and inert ingredients are need in case of some formulations.

Rationale of developing sustained release matrix devices

- For increasing duration action of the drug.
- For decreasing the dosing frequency.
- For decreasing inter and intra subject flexibility.
- For decreasing the changes level of plasma.
- For enhancing drug usage.
- For decreasing adverse effect of drug.

Polymers used in matrix tablets[17]

There are various types of polymers which are used in making the matrix tablets depending on the physical and chemical characteristics of the drug substance to be mix into matrix system and the release of drug profile required:-

Various types of polymers used for making of matrix tablets which are given below:-

1. Hydrogels
- Polyacrylamide (PA)
- Polyethylene oxide (PEO)
- Poly-hydroxy ethyl methacrylate(PHEMA)
- Cross-linked polyvinyl pyrrolidone (PVP
- Cross-linked Polyvinyl alcohol (PVA)

2. Soluble polymers
- Polyvinyl pyrrolidone(PVP)
- Polyethylene glycol (PEG)
- Hydroxypropylmethyl cellulose (HPMC)
- Polyvinyl alcohol (PVA)

3. Biodegradable polymer
- Polyanhydrides
- Polyglycolic acid (PGA)
- Polyorthoesters
- Polylactic acid(PLA)
- Polycaprolactone (PCL)

4. Non –biodegradable polymers
- Ethylcellulose (EC)
- Poldimethyl siloxane (PDS)
- Cellulose acetate (CA)
- Polyether urethane (PEU)
- Polyetylene vinyl acetate (PVA)
- Polyvinyl chloride

5. Natural Gums
- Gum Arabic
- Guar gum
- Locust bean gum
- Xanthan gum

- Karaya gum

6. Mucoadhesive polymers
- Pectin
- Tragacanth
- Sodium carboxymethyl cellulose
- Methylcellulose
- Polyacrylic acid
- Polycarbophil

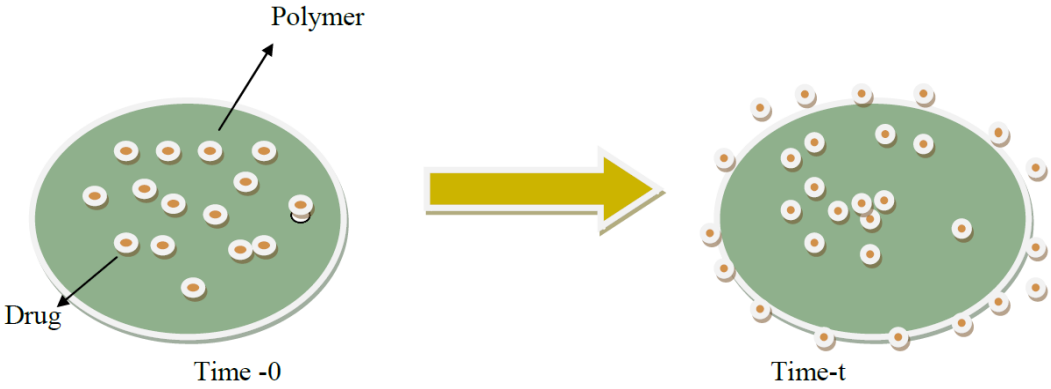

Fig. Drug Release from polymer matrix tablet.

Terminology
Sustained and controlled release, both have been used in incompatible and complicated way. Both together display different process of delivery. Sustained release establish any dosage form which provide medication over a prolong time or it indicates that the system is able to give some actual control of therapeutic.

Modified drug release products
Modified release of drug products describes drug products that modify the time or release rate of drug substance.

Extended release dosage forms
These are formulate for continuing of drug activity for longer duration of time as compared to conventionals drugs.
Examples –sustained release, controlled release.

Control release
In this drug is deliver from the drug system at a predetermined rate over a long duration of time.

Sustained release
In this, deliver of drug from drug system that attains drug release over long duration of time but not particularly at a predetermined rate.

Prolong actions dosage forms
It is plan to releasing the drug slowly and providing a continuous drug supply over a long duration of time.

Types of matrix system
These are divided into five categories on the basis of types of retarding materials or polymeric materials
1. Biodegradable matrix sstem
2. Hydrophobic matrix system
3. Mineral matrix system
4. Fat wax matrix system
5. Hydrophilic matrix system

1. Biodegradable matrix system
These matrices are made up of monomers. These are linked with each other though functional groups and has an unstable linkage. These are biologically decomposed by generated enzymes by surroundings living cells or non-enzymatic process convert into monomers and oligomers which can be metabolized or excreted.[20]
Examples of natural polymers are polysaccharides
Examples of synthetic polymers are aliphatic polymesters, polyanhydrides.

2. Mineral matrix system
These polymers are obtained from various species of seaweeds which are used to prepare mineral matrices.
Examples –Hydrophilic carbohydrate (alginic acid) obtained from brown seaweeds (Phaephyceae) by the help of dilute alkali.

Classification based on porosity of matrices are :-
i. Microporous system
ii. Non porous system
iii. Macroporous system

i. Microporous system:- In case of microporous system, pore size ranges between 50-200 A^0 through which diffusion takes places.
ii. Non-porous system –In non-porous system, there is no pores are found and by the help of molecules are diffuses.
iii. Macroporous system:- In macroporous system, pores size ranges between 0.1µm to 1µm through which diffusion takes place.[21]

3. Hydrophobic matrix system (plastic matrices):- The term of using hydrophobic or material (Inert) as matrix material was first used in 1959. In this, rate controlling components of hydrophobic is nature of water insoluble.

These ingredients consists of waxes, fatty acids, glycerides and polymeric materials include methylcellulose and ethylcellulose. In this matrix tablet, the mechanism of drug release is diffusion. This type of matrix tablets is inert in the present of Gastrointestinal fluid and water. Hydrophobic matrix ststem in the addition gives predetermined delivery rate has becoming very important.

4. Fat wax matrix system:- By the help of spray congealing in the air, the drug mix with fat wax granulation blend congealing in aqueous media in presence of not presence the alter of a spray drawing methods and surfactant. By the help of compacting with roller compactor, the mixture of drug ingredients waxy matrials and fillers are converted into granules by heating in a suitable mixture like as fluidized bed and a steam jacketed blender and a solution with granulation of waxy material and other binders. The drug is fix with a fat and waxes released by hydrolysis as well as the fats dissolution in influence of change in PH and enzyme in GIT Tract. In addition of surfactants in the formulation influence the proportion of total amount of drug and rate of drug release that mix with matrix.[19]

5:- Hydrophilic matrix system:- Matrix system within polymer(hydrophilic) are mostly used in oral controlled drug delivery due to their compliance for obtaining a beneficial release drug profile, low cost effective. Hydrophilic matrices preparation, following Polymers used which are given below.

A:-Polymers of acrylic acid:- Acrylic acid group polymers is carbopol 934. In the prepation of matrix tablet hydrophilic matrix tablet hydrophilic materials are used such as Alginic acid, Natural Gum and Gelatin.

B:-Semi-synthetic or Non-cellulose natural Polymers:- Examples includes Alginates galactose, chitosan, Modified starches and, carob, gum.

C:- Derivates of cellulose:-Examples includes such as sodium Carboxy methyl Cellulose, Hydroxy ethyl cellulose, Methyl cellulose. 400 and 400cPs, Hydroxy propyl methyl cellulose(HPMC) 25,100,400 and 15000cPs.

Table 1:- Retardant Material used in preparation of matrix Tablet are of two classes which are given below.

Sr. No.	Matrix Characteristics Material
1.	Erodible, Insoluble Ethyl cellulose, Polyvinyl chloride (PVC)
2.	Inert Insoluble Polyethylene glycol (PEG), Stearic acid.

Drug release rate from matrix system can be effect by different factors which are given below

Drug release from polymers matrix system is depend on the physical and chemical property of drug and polymers and also depend on biological factors which are given below[21]:-

1. Physical factors and chemical factors

1. Polymer swelling property.
2. Effect of diluents.
3. Dose of drug loading.
4. Size of dose.
5. Additives or Pharmaceutical aids.
6. Partition coefficient.
7. Stability.
8. Ionization, PKa and aqueous solubility.
9. The thickness of hydrodynamic diffusion layer.
10. Thickness of polymer diffusional path.
11. Diffusivity of polymer.
12. Solubility.
13. Solubility of drug.
14. Surface area and volume.
15. Polymer viscocity.

1. Polymer swelling property:- Dissolution of polymer includes such as adsorption or absorption of water in more accessible places, break down of Polymer – Polymer linkage with formation of water polymer linking, Polymers chain separation, swelling by dispersion of polymeric chain in medium of dissolution. Hydration of polymer and Swelling process in polymer study is required.

2. Effect of diluents:- Diluent or filler effect depend on diluents nature. Lactose (soluble in water) purpose is marked to increase in drug rate of release and mechanism of release has been shifted in relation to Fickian diffusion. Dicalcium Phosphate(Insoluble diluents) decreases the Fickian diffusion and also increase the erosion matrix rate. Filler(Soluble in water) matrices increase the penetration into inner part of matrix, heads to increase in hydrophilicity of System, which leads to increase in diffusion of drugs thus also increased in release rate of drug.

3. Dose of drug loading:- The dose of loading drug has a remarkable effect on kinetics of release with the solubility of drug. In case of poorly soluble drugs, the initial drug loading release kinetics is more complex. Freely(Water soluble drug), matrix porosity depend upon increase in depletion in the increase initial amount of drug loading.

4. Additives or Pharmaceutical aids:- On addition of non-polymeric excipients with polymeric material has been claimed for producing increasing in releasing rate of soluble(Water) active principles. This leads to increase in rate of release would be remarkable if additives are soluble such as lactose and very less important if the pharmaceuticals aids are not soluble such as tricalcium phosphate.

5. Partition coefficient:- Oil soluble drugs partition coefficient is becomes very important in the

determination of membrane barrier penetration effectiveness. Lipophilic nature compound has high partition coefficient are poorly aqueous. Sustain release drug delivery is not need for retaining in the lipophilic tissue for longer duration of time.

6. Size of dose:- In oral administration of drug, the upper limit to size of bulk dose to be administered. Compounds having large dose size should be given in multiple amount or prepared into system of liquid.

7. Aqueous solubility, pKa and ionization:- Moat of the drugs are weak aides and bases. Delivery system of drug are depend upon dissolution or diffusion and also depend on solubility of drug in media of aqueous.

8. Stability:- Oral administration of drug can given to acid base hydrolysis and degradation of enzymes. Dosage form, which are unstable in the stomach prolong delivery in the entire course transit in tract of Gastro-intestinals it is also available for the slow release of dosage form that enters into the small intestine. Some compounds not stable in small intestine may lead to decreased bioavailability, when sustained dosage form of drug is administered. Because more drugs are deliverd in small intestine, therefore subject to degradation. Such drugs examples are propantheline and probanthine.

9. Thickness of polymer diffusional path:-Matrix type and capsule type of polymeric drug delivery of controlled relase of drug is governed by fick's law of diffusion :-

JD=Ddc/dx

Where, JD is flux of diffusion across a plane surface of unit area.
D= Drug molecule diffusibility
dc/dx=concentration gradient of drug molecule across a diffusion path with thickness dx.

10. The thickness of hydrodynamic diffusion layer:- On increasing the thickness of hydrodynamic diffusion layer leads to decrease in the magnitude of drug release value.

11. Solubility:- By the help of new perfusion, the invivo sink maintained of drug release. By the help of perfect sink condition invitro drug release studies are conducted.

12. Drug solubility:- Water solubility and molecular size of drug factors in the drug release from erosion and swelling of controlled matrices (polymer).

13. Diffusitivity of polymer:- Small polymer molecule diffusion is energy activated process in that the molecules of diffusing molecules start moving to a successive equilibrium position whenever small amount of activation of energy for diffusion.

Biological factors
1. Metabolism
2. Absorption
3. Biological Half life
4. Protein binding
5. Distribution
6. Margin of safety

1. **Metabolism:-** Before absorption, some drugs are metabolized, in each tissue and lumen of the intestine, it showing decreasing in bioavailabiltity from the slower-releasing dosage form.

2. **Absorption:-** In the absorptive area of Tract of Gastrointestinal of any drug has transit time is about 8 hours to 12 hours. Half life (Maximum) for absorption should be approx 3 hours to 4 hours. Apart from that, the device will leads to passing out of the potential absorptive area before release of drug is complete. One of the method for providing the sustain mechanism of delivering for compound trying to maintain them within the stomach which allows slowly-slowly release of drug, then it travels to the absorptive sit. Use of bioadhesive materials is an another best approach.

3. Biological half life:- Each and every drug has elimination rate, which has the sum of all elimination process, which includes urinary excretion, chemical change of drug from one form to another (Metabolism) and including all the process remove the drug from bloodstream. For sustained release, compound with short half life is excellent candidate.

Drug release kinetics from sustained release matrix system
1. Higuchi's model
2. Zero-order kinetics
3. First order kinetics

1. Higuchi's model:- Higuchi's equation described the release of drug from matrix device by diffusion.

$Q= \sqrt{D\ \delta/\tau(2C- \delta Cs)Cst}$

Where Q= At time 't' amount of release of drug
D = Diffusion coefficient of the drug in the matrix.
Cs= Solubility of the drug in the matrix.
δ = Porosity of matrix
τ =Tortuosity
T= time(h)

Equation may be simplified then the equation becomes:-

$Q=K_H X\ t^{1/2}$

Where KH= Higuchi dissolution constant
Whenever data are plotted according to this equation, i.e. cumulative released of drug VS Square roof of time, gives a straight line, it indicates that the drug was released by mechanics of diffusion controlled.

3. Zero-order kinetics:- By the help of following equation A Zero-order release would be predicted:-

$$Q_t-Q_0=K_0t$$

Where Qt=Amount of drug release dissolved in time't'
Qo=Initial amount of drug concentration in solution.
Kot=Zero-order rate constant.

Whenever data are plotted as cumulative % of drug release VS time, if the plot is linear. Then data follow Zero-order kinetics with slope Ko. For achieving the prolonged pharmacological action this model represents an ideal drug release profile.

3. First order kinetics:- By the help of following equation, First order release would be predicted.
Log Qt=logQo-K1t/2.303

Where:- Qt = Amount of drug release in time't'
Qo= Initial amount of drug concentration in solution.
K1t= First order rate constant
Whenever data were plotted as log cumulative % of drug remaining VS time, gives straight line which indicates that the release follows first order kinetics.
The constant release rate, K can be obtained by multiplying values of slope.[22]

Drug suitable to be formulated as matrix tablets
Drugs with short half life (<5hours). Water soluble (freely) and have therapeutic window (large) can be prepared as sustained release matrix system. The Drugs with suitable polymer and combination of Polymers to prepare matrix are enlisted in table 2 :-

Table 2:- Combination of some drugs and polymers prepared into matrix tablets

Drugs	Polymers
Tramadol	Gum Damar, Gum Copal, HPMC-K4M, Karaya Gum
Theophylline	Carbopol -934P, HPMC-K100M
Acarbose	HPMC, Eudragit
Furosemide	Guar gum, Xanthan Gum, Pectin,
Aceclofenac	Guar Gum HPMC-K4M
Metformin Hcl	HPMC-K100M.EC
Ibuprofen	EC, CAP
Domperidone	HPMC-K4M, Carbopol-934P
Indomethacin	EC, HPMC, Guar Gum, Gum copal
Chlorpheniramine Meleate	Xanthan Gum, Chitosan
Minocycline	HPMC-K4M, HPMC-K15M,EC
Losartan potassium	HPMC-K100M, HPMC-K4M

CONCLUSION
From the above discussion it can be concluded that, sustained released matrix tablet developed by the help rational combination of polymers for increasing the efficiency of drug and also helpful in improving patient's compliance. The systems are economical since these systems are formed by the help of commonly available polymers. These systems are helpful in constant delivery of drug for a longer period of time in patients who needs.

REFERENCES

1. Kumar S, Kumar A, Gupta V, Malodia K, Rakha P. Oral extended release drug delivery system: a promising approach. Asian J Pharm Technol, 2012; 2: 38-43.
2. Yang Lina S, Kawashimab Y.Current status and approaches to developing press-coated chronodelivery drug systems. J Controlled Release, 2012; 157: 331-53.
3. Sharma A, Sharma S, Jha KK. The study of salbutamol matrix tablets using different polymers as release retarding agent. Pharma Res., 2009; 1: 15-22.
4. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and their *in vivo* success: a recent update. Asian J Pharm Sci., 2016; 11: 575–84.
5. Das MK, Sahu BP, Hazarika JNR. Development of bilayer tablets for the immediate and controlled release of allicin. Int J Curr Pharm Res., 2017; 9: 153-60.
6. Ain S, Kumar B, Pathak K. Development and characterization of controlled release famotidine matrix tablets containing complexes. Int J Appl Pharm, 2017; 9: 38-46.
7. Rajput GC, Majmudar FD, Patel JK, Thakor RS, Patel BP, Rajgor NB. Stomach-specific mucoadhesive microsphere as a controlled drug delivery system. Int J Pharm Biomed Res., 2010; 1: 30-41.
8. Olivares-Morales A, Kamiyama Y, Darwich AS, Aarons L, Rostami-Hodjegan A. Analysis of the impact of controlled release formulations on oral drug absorption, gut wall metabolism and relative bioavailability of CYP3A substrates using a physiologically-based pharmacokinetic model. Eur J Pharm Sci., 2015; 67: 32-44.
9. Shin KH, Yoon G, Yoon IS, Park JW. Preparation and evaluation of oral controlled-release cilostazol formulation: pharmacokinetics and antithrombotic efficacy in dogs and healthy male Korean participants. J Pharm Pharmacol, 2014; 66: 961-74.
10. Neeharika MS, Jyothi BJ. Chronotherapeutics: an optimizing approach to synchronize drug delivery with circadian rhythm. J Crit Rev., 2015; 2: 31-40.
11. Kubova K, Pecek D, Hasserova K, Dolezel P, Pavelkova M, Vyslouzil J, *et al.* The influence of thermal treatment and type of insoluble poly (meth)acrylates on dissolution behavior of very soluble drug from hypromellose matrix tablets evaluated by multivariate data analysis. Pharm Dev Technol, 2017; 22: 206-17.
12. Jayanthi B, Manna PK, Madhusudhan S, Mohanta GP, Manavalan R. Per oral extended release products-an overview. J Appl Pharm Sci., 2011; 1: 50-5.
13. Li L, Zhang X, Gu X, Mao S. Applications of

natural polymeric materials in solid oral modified-release dosage forms. Curr Pharm Des, 2015; 21: 5854, 67.
14. Agüero L, Zaldivar-Silva D, Peña L, Dias ML. Alginate microparticles as oral colon drug delivery device: a review. Carbohydr Polym, 2017; 168: 32-43.
15. Semjonov K, Kogermann K, Laidmäe I, Antikainen O, Strachan CJ, Ehlers H, *et al*. The formation and physical stability of two- phase solid dispersion systems of indomethacin in supercooled molten mixtures with different matrix formers. Eur J Pharm Sci., 2017; 97: 237-46.
16. Zimmer Ł, Kasperek R, Poleszak E. Modern polymers in matrix tablets technology. Polim Med, 2014; 44: 189-96.
17. Chidambaram N, Porter W, Flood K, Qui Y. Formulation and characterisation of new layered diffusional matrices for zero- order sustained release. J Controlled Release, 1998; 52: 149-58.
18. Zou M, Wang Y, Xu C, Cheng G, Ren J, Wu G. Wax-matrix tablet for time-dependent colon-specific delivery system of sophora flavescens aiton: preparation and *in vivo* evaluation. Drug Dev Ind Pharm, 2009; 35: 224-33.
19. Campiñez MD, Aguilar-de-Leyva A, Ferris C, de Paz MV, Galbis JA, Caraballo I. Study of the properties of the new biodegradable polyurethane PU (TEG-HMDI) as matrix forming excipient for controlled drug delivery. Drug Dev Ind Pharm, 2013; 39: 1758-64.
20. Kanjanabat S, Pongjanyakul T. Preparation and characterization of nicotine-magnesium aluminum silicate complex-loaded sodium alginate matrix tablets for buccal delivery. AAPS PharmSciTech, 2011; 12: 683-92.
21. Krajacic AB, Tucker G. Matrix formation in sustained release tablets: possible mechanism of dose dumping. Int J Pharm, 2003; 251: 67-78.
22. Shaikh HK, Kshirsagar RV, Patil SG. Mathematical models for drug release characterization: a review. World J Pharm Res., 2015; 4: 324-38.