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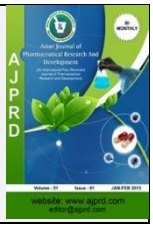

Open Access Review Article

The Role of Matrix Tablet in Oral Drug Delivery System

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A B S T R A C T

Matrix tablet is an important tool for controlled and sustained release dosage forms. The important route of drug administered by oral route. The oral dosage forms developed and improvedthe patient compliance. The oral controlled release system has been developed by change to formulation scientist, due to the inability to restrain and localized of a system at target area of the gastrointestinal tract. The hydrophilic polymers are becomes product of choice for important ingredients formulation of sustained release dosage forms.The benefit of sustained release dosage forms are compared to the conventional dosage forms and uniform therapeutic effects and drug plasma concentration. The matrices used of various class of hydrophilic, hydrophobic, mineral or biodegradabletypes of polymers and their degradation product have been focused. The drug have less half-life and eliminated from the body with in short period of time. The formulation of drug matrix types have been avoided by difficult sustained release drug delivery system. The mechanism of matrix tablets include the both dissolution and diffusion controlled. It produce the therapeutic efficacy. The goal of this review article is to discuss the release mechanism of the drug dosage form of various polymers and a matrix system used in preparation of matrix tablets.

Keywords: Types of Matrix tablets, Mechanism of Matrix tables, Drug release

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INTRODUCTION

Matrix tablet is an important tool for controlled and sustained release dosage form. The oral route are the most common route for the administration of drug. The matrix tablets have lowest cost methods to sustained and controlled release dosage forms. Hydrophilic polymer matrix are used in this dosage form. The use of different polymer in controlling release of drug has become the most important tool in the formulation of matrix tablets.The development of oral controlling release system has been a challenge to formulation scientist, due to their inability to restrain and localize the system at the target area of gastrointestinal tracts. The aim on the discussion of different material used to prepared matrix tablets, different types of matrix tablet and the drug release mechanism from the matrices.[1]

These are the type of controlled drug delivery system, which release the drug in continuous by both dissolution controlled and diffusion controlled mechanism. To control the release of drug, which are having different solubility properties, the drug is dispersed in swell able hydrophilic substance, an insoluble matrix of rigid non swell able hydrophilic material or plastic materials. Controlling drug delivery system: It define as;

- The sustained drug action at a predetermined rate by maintaining a relatively constant.
- Target drug action by using carriers or chemical derivative to deliver drug to a particular target cell type.
- Provide a therapeutically or physiological based during release system.

Pharmaceutical design for oral delivery are immediate release types/or conventional drug delivery system, in which design for immediate release of the drug for rapid absorption. They have some limitation are given

Drug with short half- life required frequent administration, which increase the change of missing dose of drug leading to poor patient's compliance.

A peak-valley plasma concentration of time profile has been obtained from which make attachment of steady state condition difficult.

The fluctuation of the drug lead to precipitation of adverse effect of drug with small therapeutic index. Whenever overmedication occurs, then, the several technical advancement have leads to the development of controlled drug delivery system that could be revolutionize method of medication a provide a number of therapeutic benefits.[3]

The matrix system of hydrophobic polymers matrix has been widely used in controlled drug delivery system and application due to their chemical inertness, cost effectiveness, regulatory acceptance and flexibility of the designed drug release profiles. Because of increased complication and expense involved in the marketing of new drug entities, greater attention has focused on the development of modified release drug delivery system. The controlled release system can be influenced by physiological condition like as motility, ions, pH and enzymes. Hydrophilic matrix systems are used for oral controlled drug delivery and they can reproduce a desirable drug profile and cost effectives. The primary mechanism of drug release from hydrophilic matrices occurs, when the polymer swells on contact with aqueous medium to form gel layer on the surface of system. The drug release by dissolution and diffusion.[4]

Advantage [4]

- Easy to manufacture
- Versatile, effective and low cost
- Made to release high molecular rate compounds.
- sustain release formulation avoided the high blood concentration
- Sustain release formulation have been the potential and improve the patient compliance.
- Reduce the toxicity
- Increase the stability by protecting the drug from hydrolysis or other derivatives change in gastrointestinal tract.
- Minimize local and systemic side effects
- Improved efficacy of drug
- Minimize the drug accumulation with chronic dosing.
- Improvement drugs bioavailability
- Provide specific effects.
- Eg: The relief of arthritis of dose of drug through bed in morning time.

Disadvantage[4]

- The remaining matrix must be removed after the drug has been released.
- High cost of production preparation
- The rate of drug release has affected by various factor like asrate transit and food through the gut.
- The rate of drug release vary with square root of the times. Release rate continuously diminishes due to an increase in diffusion front. However, a substantial sustained effect has been produced through the use of very slow release rate, which have many application are indistinguishable from zero order.
- Expensive equipment
- Poor *in vitro-in vivo* correlation.
- Stability problem
- Need for counselling and additional patients education

Polymer used in matrix tablets:

Polymer used in matrix tablet may be classified as:[13]

Hydrogel:

a) Poly-hydroxyethyl methacrylate (PHEMA)
b) Cross-linked polyvinyl alcohol (PVA)
c) Cross-linked polyvinylpyrrolidone (PVP)
d) Polyethylene oxide (PEO)
e) Polyacrylamide (PA)

Soluble polymers:

a) Polyethylene glycol
b) Polyvinylpyrrolidone (PVP)
c) Hydroxypropyl methylcellulose (HPMC)

Biodegradable polymers:

a) Polylactic acid (PLA)
b) Polyglycolic acid (PGA)
c) Polyanhydride
d) Polyorthoester

Non -biodegradable polymers:

a) Polyethylene vinyl acetate (PVA)
b) Polydimethylsiloxane (PDS)
c) Polyether urethane (PEU)
d) Polyvinyl chloride (PVC)
e) Cellulose acetate (CA)
f) Ethyl cellulose(EC)

Mucoadhesive polymers:

a) Polycarbophil
b) Sodium carboxy methylcellulose
c) Polyacrylic acid
d) Tragacanth
e) Methylcellulose
f) Pectin

Natural gums:

a) Xanthun gum
b) Guar gum
c) Karaya gum
d) Gum Arabic
e) Locust bean gum

Types of matrix tablets

The types of matrix tablet are given below:

On the basis of retardant material used

a) Hydrophobic matrix system
b) Hydrophilic matrix system
c) Fat -wax matrix system
d) Biodegradable matrix system
e) Mineral matrices

On the basis of porosity of matrix

a) Macro porous system
b) Micro porous system

c) Non porous system

Hydrophobic matrix system:

The water insoluble hydrophobic matrix are primary rate controlling component in natures. These ingredients are include waxes, glycerides, fatty acid and polymeric materials like as ethyl cellulose, methyl cellulose, and acrylate copolymers. The hydrophobic matrix system are providing programmable rate of delivery have become more important. Constant rate drug delivery always has been one of the primary target of controlled release system for the drug with narrow therapeutic index.[5,6]

Hydrophilic matrix system:

The primary rate limiting ingredients of the hydrophilic matrix polymer are swells, when a contact with the aqueous solution and form a gel layer on the surface of the system. When the release medium (i.e water) is thermodynamically compatible with a polymers, the solvent penetrates into the free space between macromolecular chains. In the relaxation process, due to stress of penetrates solvent, so that, the polymer chain are more flexible and matrix swells. The important polymers has been used in hydrophilic matrices like as HPMC(Hydroxy propyl methyl cellulose), HPC(Hydroxy propyl cellulose), xanthan gum, Carbopol 940 and alginates. HPMC and HPC polymers are unique properties and they can be display good compression characteristic include when directly compressed. They are non-toxic and high level of drug loading. They having swelling properties and allows to rapid formulation of an external gel layer, which play important role in controlled drug release.[5,6]

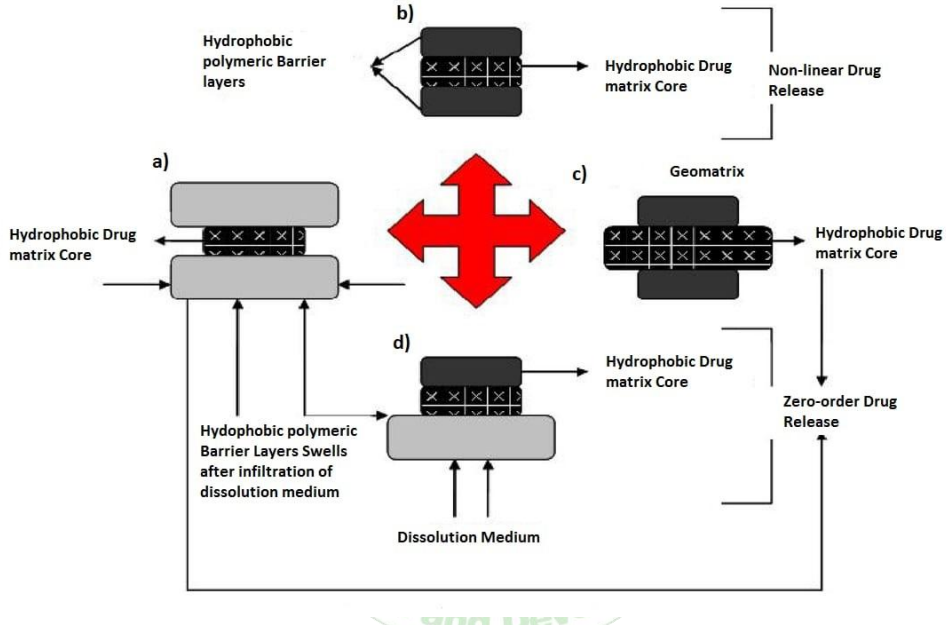

Figure: 1. Possible drug release mechanism from various matrix system.

Fat -wax matrix system:

The drug incorporated into fat wax granulation by spray congealing in the air, bleeding congealing in the aqueous media with or without the aid of the surfactant and the spray drying technique. The mixture of active pharmaceutical ingredients, wax materials and filter can be converted into granules by compacting with roller compacter, heating in suitable mixture like as fluidized bed and steam jacket blender with a solution of a wax materials or other blender. The addition of surfactant to the formulation can be also influenced both the drug release and proportion of the total drug that can being corporate into a matrix.[5,6]

Biodegradable matrix system:

These matrices of the polymersin which composed of monomers and have been linked to one another with the help of the functional groups and unstable linkage in the backbone. They have been degraded by enzyme and generated by surrounding cell or organ, non-enzymatic process into oligomers and monomers in the biological system. Example, the natural polymers like as protein,polysaccharides, modified natural polymers and synthetic polymers like as aliphatic polyesters, polyanhydrides, polycaprolactone etc.[6]

Mineral matrices:

This types of matrices are consist of polymers, which are obtained and found from various species of seaweeds. Example: Alginic acid which is a hydrophilic, carbohydrates obtained from species of brown seaweeds by use of dilute alkali.[6,7]

On the basis of porosity of matrix:

In this system, the drug molecules diffuse across the matrix and produced sustained release.

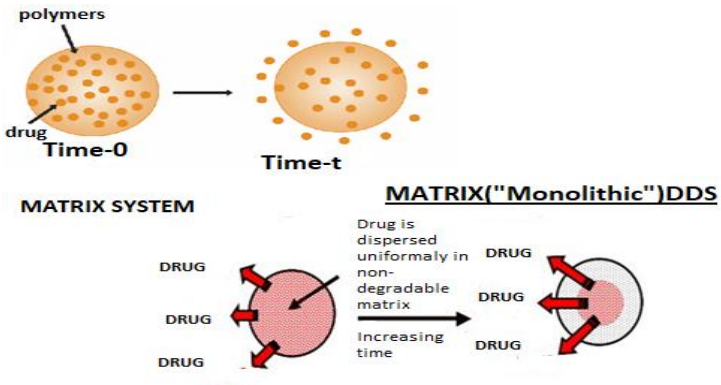

Figure: 2 Control release oral drug delivery system

Macro porous system:

In this system, the diffusion of drug occurs through pore of matrix, which size range is 0.1 to 1 micro-meter. This size is larger than the diffusion molecule size.[7,8]

Micro porous system:

In this type of system, they have been occured through pores. Micro porous system of the size range between 50 to 200A°,which is slightly larger than the diffusing molecule size.[8,10]

Non porous system:

There are no pore phase in this system. Only one polymeric phase exists and the molecules diffuse through the network meshes.[7,8,9]

Mechanism action of matrix tablets:[12,13]

Drug is the outside layer exposed to the bathing solution has been dissolved first and diffuse out of the matrix. It followed that this system to be diffusion controlled,the rate of dissolution of the drug particles within the matrix drug delivery system must be faster than the diffusion rate of dissolved drug leaving the matrix. The mathematical model of deviation has been described by this system involves the following as-

A pseudo-steady state is maintained during drug release,

The diameter of the drug particle is less than the average distance of the drug diffusion through the matrix,

The bathing solution has been provided sink condition at all times.

By equation,

$dM/dh = Co.dh - Cs/2$ ……(1)

Where,

dm=change in the amount of drug release per unit area.

dh=change in the thickness of the zone of matrix that has been depleted of drug.

Co=total amount of drug in the unit of volume of matrix.

Cs= saturated concentration of the drug within the matrix.

According to diffusion theory,

$dM = (Dm. Cs/h) dt$…… (2)

Where,

dM=diffusion coefficient in the matrix

h= thickness of drug depleted matrix

dt= change in time

By combination equation 1and 2,we get

$M = [Cs. Dm(2Co-Cs) t]^{1/2}$……(3)

When the amount drug is in excess of the saturation concentration then:

$M = [2Cs. Dm.Co.t]^{1/2}$…… (4)

Equation 3and 4 related, the amount of drug release to the square-root of time.The drug release from the porous monolithic matrix involve the penetration of surrounding liquid, dissolution of drug and leaching out of the drug trough intestinal channels and pores. The volume and length of the opening must be accounted in the drug release from a porous /granule matrix.

$M = [Ds.Ca. p/t. (2Co-p. Ca) t]^{1/2}$……(5)

Where,

P= porosity of the matrix

t= tortuosity

Ca=solubility of drug in the release medium

Ds= diffusion coefficient in the release medium

T= Diffusional path length

At pseudo steady state, the equation can be written as.

$M = [2D.Ca. Co(p/T) t]^{1/2}$…… (6)

Total porosity of matrix can be calculated by following equation

P= Pa+Ca/p+ Cex / pex…… (7)

Where,

P= porosity

P= drug density

Pa= porosity due to air pockets in the matrix

Pex= density of the watersoluble excipients

Cex= concentration of watersoluble excipients

For the purpose of data treatment,equation7can be reduced to:

$$M=k.t^{1./2} \quad \text{..... (8)}$$

Where, k= constant

The amount of drug release versus the squire root of time will be linear, if the release of drug from matrix is diffusion controlled. In this case, the controlled by varying the following parameter.

- Initial concentration of drug in the matrix
- Porosity
- Tortuosity
- Polymer system forming the matrix
- Solubility of the drug

Different factors effecting the rate of drug release from matrix system

A) Physiochemical factors [2,14, 15, 16, and 17]

Selling properties of polymers:

The polymers are dissolution includes absorption or adsorption of water in more accessible place rapture of polymers-polymer linking, separation of polymeric chain in dissolution medium. Therefore, the study of swelling polymers are required.

Drug solubility:

The molecular size and water solubility of drug are important determinants in the release of drug from swelling and erosion controlled polymers matrices. The drug with reasonable aqueous solubility, release of dosage forms occurs by dissolution infiltration medium and drug with the poor solubility release occurred by both dissolution of drug dissolution particle through erosion of matrix tablets.

Polymers hydration:

It is important part of study of polymer/hydration/swelling process for the maximum number of combination polymers and polymeric. The polymer dissolution studies, it includes absorption or adsorption of water in more accessible place, rupture of polymers-polymers linked with the forming of water polymers linking and separation polymeric chain, swelling and dispersion of polymeric chain in dissolution medium.

Polymers diffusivity:

The diffusion of small molecules are the polymers structure and energy activated process in which the diffusant molecules moves to a successive series of equilibrium position.When a sufficient amount of energy of activation. The diffusion has been acquired by the diffusant and dependent on length of polymer chain segment, cross linking and crystallinity of polymer. The release of drug attributed by the three factors are

i. Polymer particle size
ii. Polymer viscosity
iii. Polymer concentration

Polymer particle size:

Malamataris stated that when the content of hydroxyl propyl methylcellulose is higher. The effect of particle size is less important on the release rate of propranolol hydrochloride. The effect of this variable more important and when the content of polymer is low. As the result, it is considering that in certain areas of matrix containing low levels of hydroxyl propyl methylcellulose led to the burst release.

Polymer viscosity:

In this cellulose ether polymers, viscosity has been used as an indication of matrix weight and increasing the molecular weight or viscosity of the polymer in the matrix formulation increases. The viscosity of the gel layers are slows drug dissolution. The greater viscosity of the gel are more resistant of the gel to the dilution, erosion and thus, controlling the drug dissolution.

Polymer concentration:

An increase in polymer concentration, it causes an increase in the viscosity of gel as well as formulation of gel layer with a longer diffusional path. This could be cause a decrease in the effective diffusion coefficient of the drug and therefore, the reduction in drug release. The mechanism of drug release from matrix dosage forms and also changes from erosion to diffusion as the polymer concentration increases.

Thickness of polymers diffusional parts:

The controlled release of a drug from both capsule and matrix type polymeric drug delivery system is governed by Fick's law of diffusion:

$$JD = D\, dc/dx$$

Where,

JD = flux of diffusion across a plane surface of unit area

D = Diffusibility of drug molecule

dc/dx = Concentration gradient of drug molecule across a diffusion path with thickness dx.

Surface area and volume:

The rate of drug release on the surface area of the drug delivery device is well known theoretically and experimentally. Both *in vitro* and *in vivo* rate of the drug release and observed to be dependent upon surface area of dosage forms. It founded that release from small tablet is faster than large cylindrical tablets.

Diluent's effect:

The effect of diluent or filler depends upon the nature of diluent. Water soluble diluents like lactose, which cause marked by make a greater in size in drug release rate and release mechanism has been also shifted towards **Fickian diffusion**, while insoluble diluents like Dicalcium phosphate reduce the increase the relaxation (erosion) and Fickian diffusion rate of matrix. The reason behind that water soluble filler in matrices stimulate the water penetration in to inner part of matrix, due to increase in hydrophilicity of the system, it causing rapid diffusion of drug, leads to increased drug release rate.

Thickness of hydrodynamic diffusion layer:

The magnitude of drug release value is decrease on increase the thickness of hydrodynamic diffusion layer.

Drug loading dose:

The effect of initial drug loading of the tablet and resulting release kinetic more complex in case of poorly water soluble drug and which increase the initial loading of the drug relative release rate first decrease and then increase, whereas, absolute release rate increase . In the case freely water soluble drug, the porosity of matrix tablets upon drug depletion increase with initial drug loading.

Additives effects:

The effect of loading non-polymeric excipient to a polymeric matrix has been claimed to produce increase in release the rate would marketed.The soluble excipients are like aslactose and insoluble excipient like as Tricalcium phosphate.

Ionization, PKa, aqueous solubility:

The drug are weak acid or base. The uncharged structure of a drug penetrates across the membrane of lipid. The Presenting of the drug in an uncharged form and are beneficialfor drug penetration. The compounding having a low solubility (<0.01mg/ml) are sustained .Since, their release in the GIT will be restricted by drug dissolution. The solubility of compound will be poor and slightly soluble drug.

Partition coefficient:

To produce the therapeutic effect in another area of the body, when the drug is administered to the GIT, it acrossed by the biological membrane. It is considered that these membrane are lipidic, therefore, the partition coefficient of oil soluble drug is important, determining the effectiveness of a membrane barrier penetration. The lipophilic nature of the compounds having partition coefficient are poorly aqueous soluble and it's retain in lipophilic tissue for the longer time. In the compound with very low partition coefficient, it is very difficult to penetrates membrane in the case of compound which having very low partition coefficient and resulting poor bioavailability. The choice of different limiting membrane is depend upon the partitioning characteristic of drug.

$$K= Co/Cw \ldots\ldots\ldots (1)$$

Where,

Co= concentration of organic phase at equilibrium

Cw=concentration of aqueous phase at equilibrium

K=equilibrium constant

Drug stability:

Orally administered drug can be subjected to both enzymatic degradation and acid and base hydrolysis. Degradation will be continue at the rate for in solid state. So, this is the favoured work of arts deliver for difficulty case.

B. Biological factors[16, 17]

Biological half- life:

The aim of an oral SR (sustained release) preparation is maintain therapeutic blood levels over the prolonged period of time. It enter the blood circulation at the same rate at which and it is eliminated. The eliminated rate has been described by the term half-life (t1/2). Each drug having its specific eliminated rate, in which includes metabolism, urinary excretion and all over the process and removed by the drug from the blood stream. Drug have short half-life and the best candidate for sustained release formulation and reduced the dose frequency. Drug with the half-life shorter than 2 hours, such as furosemide drug has poor candidate for sustained release preparation. The compound with long half-life, more than 8hours not used in sustaining from due to their effect sustained. Example: phenytoin and Digoxin

Absorption:

The goal of this SR(sustained release) produced bycontrol the rate of drug is much slower than the rate of the absorption. The extreme half -life for absorption should be in the region of 3-4 hours and we presumed that the transit time of the drug in the absorptive area of the GI tract is about 8-12 hoursOtherwise, the absorptive regions of dosage forms will pass out before drug release is completed. Thus, correspond to a minimum apparent absorption rate constant of 0.17-0.23 hours to give 80-95% over this time period. So that, it ca be accepted absorption of drug should occurs of a relatively uniform rate over the entire length of small intestine. If a drug has been absorbed by active transport is restricted by the specific region of intestine, SR(sustained release) preparation have disadvantage to absorption.

Metabolism:

The absorption of drug metabolism in the lumen or the tissue of intestine,slow low bioavailability and slow release rate. The criteria of the drug to be used for formulating sustained release dosage form drug should be:

- Have low half- life(<5hrs)
- Free soluble in water
- Longer therapeutic window
- The GIT Absorbed through the

Distribution:

The distribution of drug molecules into tissue and the cell can be primary factor in particularly drug elimination kinetics. The drug molecules are bind to protein and considered to be inactive to permeated that the biological membrane. The high degree of protein binding gives pronged release of drug. The apparent volume of distribution of a drug is the bioavailability. The portioning effects apply equal to distribution through polymer membrane.

Protein binding:

The pharmacological response has been unbounded the drug concentration is important than band to same extend to plasma or tissue protein. The protein binding of the drug, which show the important role of its therapeutic effects in spite of types of dosage form as extensive binding to plasma increase biological half-life. Thus, same time SR (sustained release) drug delivery system is not required for this type.

Margin of safety:

The safety of the drug depend upon the therapeutic index and large value of therapeutic index of drug safer is the drug. The drug having poor candidate and less therapeutic index for SR(sustained release) drug delivery system.

CONCLUSION

The goal of this review article has been of the formulation sustained release matrix tablets. The matrix tablets are increase the dose and helpful. The cost of production of matrix tablets is also under the control, due to the use of these tablet the daily required frequency of the dose was also reduced. The matrix tablets of drug have limiting release and various factor and mechanism. The mechanistic model have been discussed and it is concluded that HPMC polymers is widely used in all polymers due to its specific characteristic matrix tablets are the economical dosage forms improved the patients compliance, reduce dose frequency, minimum plasma fluctuation, increase the bioavailability of drug. The system are useful in the care of the patients, who need a constant deliver of the drug for a longer period of times.

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