



A REVIEW ARTICLE ON SUSTAINED RELEASE MATRIX TYPE DRUG DELIVERY SYSTEM

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ABSTRACT

The oral route is the most frequently used route for the administration of drugs. Many of the pharmaceutical dosage form are formulated as sustained release dosage form to retard the release of a therapeutic agent such that its appearance in the systemic circulation is prolonged and its plasma profile is sustained in duration. Matrix tablets serves as an important tool for oral extended- release dosage forms. Hence, problems like patient compliance, drug targeting, local side effects, frequent administration and fluctuations in blood concentration levels. Oral extended release drug delivery system becomes a very promising approach for those drugs that are given orally but having the shorter half-life and high dosing frequency. Extended-release drug-delivery system reduces the dosing frequency of certain drugs by releasing the drug slowly over an extended period of time Matrix tablets may be formulated by wet granulation or direct compression methods by dispersing solid particles within a porous matrix formed of hydrophilic and hydrophobic polymers. The use of different classes of polymers in controlling the release of drugs has become the most important aspect in the formulation of matrix tablets. The drug release in matrix drug delivery systems by both dissolution-controlled as well as diffusion controlled mechanisms.

KEYWORDS: Direct compression, extended-release, hydrophilic and hydrophobic polymers, matrix tablets, wet granulation.

INTRODUCTION

The oral route is the most popular route used for administration of drugs, which is due in part to the ease of administration and to the fact that gastrointestinal physiology offers more flexibility in dosage form design than most other routes.^[1] The terms Sustained release, prolonged release, modified release, extended release or depot formulations are used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.^[2]

Matrix tablets is a promising approach for the establishment of extended-release drug therapy as tablets offer the lowest cost approach to sustained and controlled release solid dosage forms. Matrix tablets may be defined as the “oral solid dosage forms in which the drug or active ingredient is homogeneously dispersed throughout the hydrophilic or hydrophobic matrices which serves as release rate retardants”. These systems

release drug in continuous manner by dissolution-controlled and diffusion-controlled mechanisms. Under gastric pH conditions, matrix tablet slowly erodes. However at a pH corresponding to the upper small intestine, the tablet disintegrates rapidly to reduce coated particles, which in turn slowly releases drug. Two different release mechanisms are operative, either of which is zero-order erosion and decreasing surface area, and dissolution of coated particles, but the overall tablet release profile comprising the two mechanisms in sequence is nearly linear for most of the dose in the tablet. The result in the ability to control active pharmaceutical ingredient's blood level's in a narrow range, above the minimum effective level and below toxic level. This type of sustained-release tablet has clearly shown the potential of the tablet as a reliable sustained release dosage form with good release profile precision.^[3]

Introduction of matrix tablet as sustained release (SR) has given a new breakthrough for novel drug delivery

system (NDDS) in the field of Pharmaceutical technology. It excludes complex production procedures such as coating and pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in the preparations. One of the least complicated approaches to the manufacture of sustained release dosage forms involves the direct compression of blend of drug, retardant material and additives to formulate a tablet in which the drug is embedded in a matrix of the retardant. Alternatively drug and retardant blend may be granulated prior to compression.^[4-7]

Advantage of Matrix Tablet

1. Easy to manufacture.
2. Versatile, effective and low cost.
3. Can be made to release high molecular weight compounds.
4. The sustained release formulations may maintain therapeutic concentrations over prolonged periods.
5. The use of sustain release formulations avoids the high blood concentration.
6. Sustain release formulations have the potential to improve the patient compliance.
7. Reduce the toxicity by slowing drug absorption.
8. Increase the stability by protecting the drug from hydrolysis or other derivative changes in gastrointestinal tract.
9. Minimize the local and systemic side effects.
10. Improvement in treatment efficacy.
11. Minimize drug accumulation with chronic dosing.
12. Usage of less total drug.
13. Improvement the bioavailability of some drugs.
14. Improvement of the ability to provide special effects. Ex: Morning relief of arthritis through bed time dosing.^[8-9]

Disadvantages of Matrix Tablet

1. The remaining matrix must be removed after the drug has been released.
2. Greater dependence on GI residence time of dosage form.
3. Increased potential for first-pass metabolism.
4. Delay in onset of drug action.
5. Release rates are affected by food and the rate transit through the gut.
6. Release rate continuously diminishes due to increased diffusional resistance and decrease in effective area at the diffusion front.^[8-9]

Classification of Matrix Tablets

On the basis of release retardant material used matrix tablets can be divided in to five types:

1. Hydrophobic Matrices (Plastic matrices)

The concept of using hydrophobic or inert materials as matrix materials was first introduced in 1959. In this method of obtaining sustained release from an oral dosage form, drug is mixed with an inert or hydrophobic polymer and then compressed in to a tablet. Sustained release is produced due to the fact that the dissolving

drug has diffused through a network of channels that exist between compacted polymer particles. Examples of materials that have been used as inert or hydrophobic matrices include polyethylene, polyvinyl chloride, ethyl cellulose and acrylate polymers and their copolymers. The rate controlling step in these formulations is liquid penetration into the matrix. The possible mechanism of release of drug in such type of tablets is diffusion. Such types of matrix tablets become inert in the presence of water and gastrointestinal fluid.

2. Lipid Matrices

These matrices prepared by the lipid waxes and related materials. Drug release from such matrices occurs through both pore diffusion and erosion. Release characteristics are therefore more sensitive to digestive fluid composition than to totally insoluble polymer matrix. Carnauba wax in combination with stearyl alcohol or stearic acid has been utilized for retardant base for many sustained release formulation.

3. Hydrophilic Matrices

Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery because of their flexibility to obtain a desirable drug release profile, cost effectiveness, and broad regulatory acceptance. The formulation of the drugs in gelatinous capsules or more frequently, in tablets, using hydrophilic polymers with high gelling capacities as base excipients is of particular interest in the field of controlled release. Infact a matrix is defined as well mixed composite of one or more drugs with a gelling agent (hydrophilic polymer). These systems are called swellable controlled release systems. The polymers used in the preparation of hydrophilic matrices are divided in to three broad groups:

- A. Cellulose derivatives:** Methyl cellulose 400 and 4000 cPs, Hydroxyethylcellulose, Hydroxypropylmethyl cellulose (HPMC) 25, 100, 4000 and 15000cPs, and sodium carboxymethylcellulose.
- B. Non cellulose natural or semi synthetic polymers:** Agar-Agar; Carob gum; Alginates; Molasses; Polysaccharides of mannose and galactose, Chitosan and Modified starches.
- C. Polymers of acrylic acid:** Carbopol-934, the most used variety.

4. Biodegradable Matrices

These consist of the polymers which comprised of monomers linked to one another through functional groups and have unstable linkage in the backbone. They are biologically degraded or eroded by enzymes generated by surrounding living cells or by non enzymatic process in to oligomers and monomers that can be metabolized or excreted. Examples are natural polymers such as proteins and polysaccharides; modified natural polymers; synthetic polymers such as aliphatic poly (esters) and polyanhydrides.

5. Mineral Matrices

These consist of polymers which are obtained from various species of seaweeds. Example is Alginic acid which is a hydrophilic carbohydrate obtained from species of brown seaweeds (Phaeophyceae) by the use of dilute alkali.^[10-12]

Classification on The Basis of Porosity of Matrix

Matrix systems can also be classified according to their porosity and consequently, Macro porous; Micro porous and Non-porous systems can be identified:

1. Macro porous systems

In such systems the diffusion of drug occurs through pores of matrix, which are of size range 0.1 to 1 μm . This pore size is larger than diffusant molecule size.

2. Micro porous System

Diffusion in this type of system occurs essentially through pores. For micro porous systems, pore size ranges between 50 – 200 $\text{\AA}$, which is slightly larger than diffusant molecules size.

3. Non-porous System

Non-porous systems have no pores and the molecules diffuse through the network meshes. In this case, only the polymeric phase exists and no pore phase is present.^[13-16]

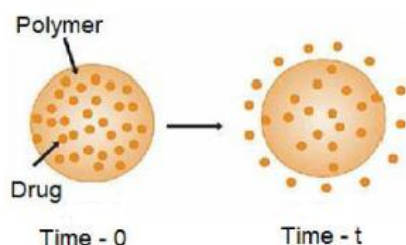


Figure: Schematic representation of diffusion across the Matrix.

Polymers used in Matrix Tablets

There are number of polymers which may be used to formulate matrix tablets depending on the physicochemical properties of the drug substance to be incorporated into matrix system and type of drug release required.^[17]

Polymers used for matrix tablets may be classified as

- A. Hydrogels polymer:** Poly-hydroxyethylene methacrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Cross-linked Polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA).
- B. Soluble polymers:** Polyethylene glycol (PEG), polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC).
- C. Biodegradable polymers:** Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), Polyanhydrides, Polyorthoesters.

D. Non-biodegradable polymers: Polyethylene vinyl acetate (PVA), Polyether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC).

E. Mucoadhesive polymers: Polycarbophil, Sodium Carboxymethyl cellulose, Tragacanth, Methyl cellulose, Pectin.

F. Natural gums: Xanthan gum, Guar gum, Karaya gum, Gum Arabic, Locust bean gum.

Mechanism of Drug Release from Matrix Tablet

Drug in the outside layer exposed to the bathing solution is dissolved first and then diffuses out of the matrix. This process continues with the interface between the bathing solution and the solid drug moving toward the interior. It follows that for this system to be diffusion controlled, the rate of dissolution of drug particles within the matrix must be much faster than the diffusion rate of dissolved drug leaving the matrix.^[18-20]

Derivation of the mathematical model to describe this system involves the following assumptions:

- a. A pseudo-steady state is maintained during drug release,
- b. The diameter of the drug particles is less than the average distance of drug diffusion through the matrix,
- c. The bathing solution provides sink conditions at all times.

The release behaviour for the system can be mathematically described by the following equation:

$$dM/dh = C_0 \cdot dh - C_s/2 \dots\dots\dots (1)$$

Where,

dM = Change in the amount of drug released per unit area

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

C_0 = Total amount of drug in a unit volume of matrix

C_s = Saturated concentration of the drug within the matrix.

Additionally, according to diffusion theory:

$$dM = (D_m \cdot C_s / h) dt \dots\dots\dots (2)$$

Where,

D_m = Diffusion coefficient in the matrix.

h = Thickness of the drug-depleted matrix

dt = Change in time

By combining equation 1 and equation 2 and integrating:

$$M = [C_s \cdot D_m (2C_0 - C_s) t]^{1/2} \dots\dots\dots (3)$$

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

$$M = [2C_s \cdot D_m \cdot C_0 \cdot t]^{1/2} \dots\dots\dots (4)$$

Equation 3 and equation 4 relate the amount of drug release to the square-root of time. Therefore, if a system is predominantly diffusion controlled, then it is expected that a plot of the drug release vs. square root of time will

result in a straight line. Drug release from a porous monolithic matrix involves the simultaneous penetration of surrounding liquid, dissolution of drug and leaching out of the drug through tortuous interstitial channels and pores.

The volume and length of the openings must be accounted for in the drug release from a porous or granular matrix:

$$M = [D_s \cdot C_a \cdot p/T \cdot (2Co - p \cdot Ca) t]^{1/2} \dots\dots\dots (5)$$

Where,

p = Porosity of the matrix

t = Tortuosity

Ca = solubility of the drug in the release medium

Ds = Diffusion coefficient in the release medium.

T = Diffusional path length

For pseudo steady state, the equation can be written as:

$$M = [2D \cdot C_a \cdot Co (p/T) t]^{1/2} \dots\dots\dots (6)$$

The total porosity of the matrix can be calculated with the following equation:

$$p = p_a + C_a / \rho + C_{ex} / \rho_{ex} \dots\dots\dots (7)$$

Where,

p = Porosity

ρ = Drug density

p_a = Porosity due to air pockets in the matrix

ρ_{ex} = Density of the water soluble excipients

C_{ex} = Concentration of water soluble excipients

For the purpose of data treatment, equation 7 can be reduced to:

$$M = k \cdot t^{1/2} \dots\dots\dots (8)$$

Where, k is a constant, so that the amount of drug released versus the square root of time will be linear, if the release of drug from matrix is diffusion-controlled. If this is the case, the release of drug from a homogeneous matrix system can be controlled by varying the following parameters:

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

Biological Factors Influencing Release from Matrix Tablet

1. Biological half life: SR product aims to maintain therapeutic blood levels over an extended period of time. In order to achieve this, drug must enter the circulation at approximately the same rate at which it is eliminated. The elimination rate is quantitatively described by the half-life ($t_{1/2}$). Each drug has its own characteristic elimination rate, which is the sum of all elimination processes, including metabolism, urinary excretion and all over processes that permanently remove drug from the blood stream. Therapeutic compounds with short half-life are

generally are excellent candidate for SR formulation, as this can reduce dosing frequency. In general, drugs with half-life shorter than 2 hours such as furosemide or levodopa are poor candidates for SR preparation. Compounds with long half-lives, more than 8 hours are also generally not used in sustaining form, since their effect is already sustained. E.g. Digoxin and phenytoin.

2. Absorption: Since the purpose of forming a SR product is to place control on the delivery system, it is necessary that the rate of release is much slower than the rate of absorption. If we assume that the transit time of most drugs in the absorptive areas of the GI tract is about 8-12 hours, the maximum half-life for absorption should be approximately 3-4 hours; otherwise, the device will pass out of the potential absorptive regions before drug release is complete. Thus corresponds to a minimum apparent absorption rate constant of 0.17-0.23 to give 80-95% over this time period. Hence, it assumes that the absorption of the drug should occur at a relatively uniform rate over the entire length of small intestine. If a drug is absorbed by active transport or transport is limited to a specific region of intestine, SR preparation may be disadvantageous to absorption. One method to provide sustaining mechanisms of delivery for compounds tries to maintain them within the stomach. This allows slow release of the drug, which then travels to the absorptive site. These methods have been developed as a consequence of the observation that co-administration results in sustaining effect.

3. Metabolism: Drugs those are significantly metabolized before absorption, either in the lumen or the tissue of the intestine, can show decreased bioavailability from slower-releasing dosage form. Hence, criteria for the drug to be used for formulating SR dosage form are:

- Drug should have short half-life (2-4 hrs.).
- Drug should be soluble in water.
- Drug should have large therapeutic window.
- Drug should be absorbed throughout the GIT.

Even a drug that is poorly water soluble can be formulated in SR dosage form. For the same, the solubility of the drug should be increased by the suitable system and later on that is formulated in the SR dosage form.

4. Distribution: Drugs with high apparent volume of distribution, which influence the rate of elimination of the drug, are poor candidate for oral SR drug delivery system e.g. Chloroquine.

5. Protein Binding: The Pharmacological response of drug depends on unbound drug concentration drug rather than total concentration and all drug bound to some extent to plasma and or tissue proteins.

Proteins binding of drug play a significant role in its therapeutic effect regardless the type of dosage form as extensive binding to plasma increase biological half-life and thus sometimes SR drug delivery system is not required for this type of drug.

6. **Margin of safety:** As we know larger the value of therapeutic index safer is the drug. Drugs with low therapeutic index are usually poor candidate for formulation of oral SR drug delivery system due to technological limitation of control over release rates.^[21-23]

Physicochemical Factors Influencing Release from Matrix Tablet

1. **Dose size:** For orally administered systems, there is an upper limit to the bulk size of the dose to be administered. In general, a single dose of 0.5-1.0g is considered maximal for a conventional dosage form. This also holds true for sustained release dosage form. Compounds that require large dosing size can sometimes be given in multiple amounts or formulated into liquid systems. Another consideration is the margin of safety involved in administration of large amount of a drug with a narrow therapeutic range.
2. **Ionization, *pka* and aqueous solubility:** Most drugs are weak acids or bases. Since the unchanged form of a drug preferentially permeates across lipid membranes, it is important to note the relationship between the *pka* of the compound and the absorptive environment. Presenting the drug in an unchanged form is advantageous for drug permeation. Delivery systems that are dependent on diffusion or dissolution will likewise be dependent on the solubility of the drug in aqueous media. These dosage forms must function in an environment of changing pH, the stomach being acidic and the small intestine more neutral, the effect of pH on the release process must be defined. Compounds with very low solubility (<0.01mg/ml) are inherently sustained, since their release over the time course of a dosage form in the GI tract will be limited by dissolution of the drug. So it is obvious that the solubility of the compound will be poor choices for slightly soluble drugs, since the driving force for diffusion, which is the drug's concentration in solution, will be low.
3. **Partition Coefficient:** When a drug is administered to the GI tract, it must cross a variety of biological membranes to produce a therapeutic effect in another area of the body. It is common to consider that these membranes are lipidic; therefore the partition coefficient of oil-soluble drugs becomes important in determining the effectiveness of membrane barrier penetration. Compounds which are lipophilic in nature having high partition coefficient are poorly aqueous soluble and it retain in the lipophilic tissue for the longer time. In case of compounds with very low partition coefficient, it is

very difficult for them to penetrate the membrane, resulting in poor bioavailability. Furthermore, partitioning effects apply equally to diffusion through polymer membranes. The choice of diffusion-limiting membranes must largely depend on the partitioning characteristics of the drug.

4. **Stability:** Orally administered drugs can be subject to both acid-base hydrolysis and enzymatic degradation. Degradation will proceed at a reduced rate for drugs in solid state; therefore, this is the preferred composition of delivery for problem cases. For the dosage form that are unstable in stomach, systems that prolong delivery over entire course of transit in the GI tract are beneficial; this is also true for systems that delay release until the dosage form reaches the small intestine. Compounds that are unstable in small intestine may demonstrate decreased bioavailability when administered from a sustaining dosage form. This is because more drugs is delivered in the small intestine and, hence, is subject to degradation. Propenteline and proanthine are representative example of such drug.^[24-26]

Effect of Various Parameters on Drug Release

Drug release kinetics may be affected by many factors such as polymer swelling, polymer erosion, drug dissolution/diffusion characteristics, drug distribution inside the matrix, drug/polymer ratio and system geometry (cylinder, sphere).^[27-28]

- A. **Drug solubility:** Water solubility of drug and molecular size is another important factor which is considered in the release of drug from swelling and erosion controlled polymeric matrices. For drugs with reasonable aqueous solubility, release of water soluble drugs occurs by dissolution in infiltrating medium and the release of poorly water soluble drug are occurs by both dissolution of drug and dissolution of drug particles through erosion of the matrix tablet.
- B. **Polymer hydration:** It is important to study polymer hydration/swelling process for the maximum number of polymers and polymeric combinations. The more important step in polymer dissolution include absorption/adsorption of water in more accessible places, rupture of polymer-polymer linkings with the simultaneous forming of water-polymer linkings, separation of polymeric chains, swelling and finally dispersion of polymeric chain in dissolution medium.
- C. **Polymer diffusivity:** The diffusion of small molecules in polymer structure is energy activated process in which the diffusant molecules moves to a successive series of equilibrium position when a sufficient amount of energy of activation for diffusion E_d has been acquired by the diffusant is dependent on length of polymer chain segment, cross linking and crystallinity of polymer. The

release of drug may be attributed to the mainly two factors.

- i. **Polymer viscosity:** Increasing the molecular weight or viscosity of the polymer in the matrix formulation increases the gel layer viscosity and thus slows drug dissolution.
 - ii. **Polymer concentration:** An increase in polymer concentration causes an increase in the viscosity of gel as well as formulation of gel layer with a longer diffusional path. This could cause a decrease in the effective diffusion coefficient of the drug and therefore reduction in drug release.
- D. **Thickness of polymer diffusional path:** The controlled release of a drug from matrix type polymeric drug delivery system is essentially governed by Fick's law of diffusion.

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

Where,

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

D = is diffusibility of drug molecule,

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

- E. **Thickness of hydrodynamic diffusion layer:** The drug release profile is a function of the variation in thickness of hydrodynamic diffusion layer on the surface of matrix type delivery devices. As the thickness of hydrodynamic diffusion layer increases, the magnitude of drug release value decreases.
- F. **Drug loading dose:** The release kinetics is significantly affected by loading dose of drug. The effect of initial drug loading of the tablets on the resulting release kinetics is more complex in case of poorly water soluble drugs, with increasing initial drug loading the relative release rate first decreases and then increases, whereas, absolute release rate monotonically increases. In case of freely water soluble drugs, the porosity of matrix upon drug depletion increases with increasing initial drug loading.
- G. **Surface area:** Both the *in vitro* and *in vivo* rate of the drug release, are observed to be dependent upon surface area of dosage form. The release of drug from small tablet is faster than large cylindrical tablets.
- H. **Effect of diluents:** The effect of diluents or filler depends upon the nature of diluents. Water soluble diluents like lactose cause marked increase in drug release rate and release mechanism is also shifted towards Fickian diffusion; while insoluble diluents like dicalcium phosphate reduce the Fickian diffusion and increase the relaxation (erosion) rate of matrix. The reason behind this is that water soluble filler in matrices stimulate the water penetration in to inner part of matrix, due to increase in hydrophilicity of the system, causing rapid diffusion of drug, leads to increased drug release rate.
- I. **Additives:** The effect of adding non-polymeric excipients to a polymeric matrix has been claimed to

produce increase in release rate of hydro soluble active principles. These increases in release rate would be marked if the excipients are soluble like lactose and less important if the excipients are insoluble like tricalcium phosphate.

Evaluation Test for Sustained Release Tablets

1. **Weight variation:** Twenty tablets were weighed individually and then collectively, average weight of the tablets was calculated.
2. **Hardness:** Hardness test was conducted for tablets from each batch using Monsanto hardness tester and average values were calculated.
3. **Friability:** The tablets were tested for friability testing using Roche friabilator, which revolves at 25rpm for 4min.
4. **Thickness:** The thicknesses of tablets were determined using micrometer screw gauge. Content Uniformity: Using UV Visible spectrophotometer found the amount of the drug using the calibration curve method.
5. **In vitro dissolution study:** Drug release study is generally determined in Rotating Paddles apparatus. Mainly buffer is used as a dissolution medium. The temperature of the bath maintained at 37°C and required sample of the dissolution medium in which drug is release is taken at a regular interval and the same quantity of the medium is replace. The amounts of the drug released is determined using an UV spectrophotometer a drug dissolved at specified time period is plot as percent release versus time.
6. **Short Term Stability Study:** To determine change in *in vitro* release profile on storage, a short term stability study of the optimal batch.^[29-31]

Kinetics of Drug Release

Zero order kinetics: Drug dissolution from pharmaceutical dosage form that does not disaggregate and drug release in slow manner represented by:

$$W_0 - W_t = K_0 t$$

Where, W_0 = Initial amount of drug concentration in solution.

W_t = Amount of drug release dissolved in time t.

$K_0 t$ = Zero order rate constant.

When the data was plotted as cumulative % drug release verses time, if the plot is linear then data obeys zero order kinetics with slope equal to K_0 . This model represents an ideal release profile in order to achieve the prolonged pharmacological action.

First order kinetics: Release of drug expressing in this model:

$$\text{Log } Q_t = \text{Log } Q_0 + K_1 t^{1/2} \cdot 303$$

here, Q_t = Amount of drug release in time t.

Q_0 = Initial amount of drug in solution.

$K_1 t$ = First order release rate constant.

When data was plotted as log cumulative % drug remaining verses time yields a straight line indicating

that the release follows first order kinetics. The constant K can be obtained multiplying slope values.

Korsmeyer Peppas model: In 1983 Korsmeyer-peppas developed a simple, semi-empiric model, when diffusion is the main drug release mechanism, relating exponentially the drug release to the elapsed time (t).

$$A_t/A_\infty = kt^n$$

Where, k = Constant.

n = Release.

t = Time.

A_t and A_∞ = Absolute cumulative amount of drug released at time (t).

This is used when the release mechanism is not well known or when more than one type of release phenomenon could be involved.

Higuchi model: Drug release from the matrix device by diffusion has been described by Higuchi's Diffusion equation:

$$ft = Q = \sqrt{D\delta / \tau (2C_s - \delta C_s)} C_{st}$$

Where, Q = Amount of drug released in time t.

D = Diffusion coefficient of the drug in the matrix.

C_s = Solubility of the drug in the matrix.

δ = Porosity of matrix.

τ = Tortuosity.

t = Time (h).

The equation may be simplified then equation becomes;

$$ft = Q = KH X t^{1/2}$$

Where, KH = Higuchi dissolution constant.

When data was plotted according to this equation, i.e. cumulative drug released verses square root of time, yields a straight line, indicating that the drug was released by diffusion mechanism.^[32-33]

List of various drugs which can be formulated as a matrix tablet with polymer and method used or its preparation are shown in table.

Drugs	Category	Method used	Polymer used
Ambroxol HCl	Secretolytic agent	Direct compression	Methocel K15MCR, PVP K30 ^[34]
Diclofenac Sodium	Anti-inflamatry	Wet granulation	Pectin, Guar gum ^[35]
Metformin hydrochloride	Antidiabetic	Direct compression	Chitosan, Ethyl cellulose HPMC, Xanthan gum ^[36]
Cefpodoxime	Antibiotic	Direct compression	HPMC (K4M), HPMC (K100M) and Xanthan gum ^[37]
Lamivudine	Antiviral	Direct compression	HPMC (Methocel K15M CR) Avicel 102 ^[38]
Terbutaline sulphate	Bronchodilator	Wet granulation	HPMC K200M, Ethyl cellulose ^[39]
Indomethacin	Anti-inflammatory	Wet Granulation	Hibiscusrosa-sinensis, Microcrystalline cellulose, Magnesium stearate ^[40]
Nateglinide	Antidiabetic	Wet Granulation	Xanthan gum, Guar gum ^[41]
Zidovudine	Anti viral	Wet granulation	HPMC, Xanthan gum, ethyl cellulose ^[42]
Furosemide	Antidiuretic	Direct Compression	Guar gum, Xanthum gum, Pectin ^[43]
Theophylline	Respiratory depressant	Wet Granulation	HPMC 15 CPS, HPMCP, Eudragit L 100, Eudragit RLPO, Polyvinyl acetate, Alginate acid ^[44]
Venlafaxine Hydrochloride	Anti-depressant	Wet Granulation	Eudragit RLPO and RSPO, Lactose ^[45]

CONCLUSION

The focus of this review article has been on the formulation of sustained-release matrix tablets, advantages and disadvantages and various polymers used to design such system. By the above discussion, it can be easily concluded that sustained-release formulation are helpful in increasing the efficiency of the dose as well as they are also improving the patient's compatibility matrix forming polymers can be successfully used to prepare Matrix tablets, releasing drug in a controlled manner. This suitability of matrix forming polymers, to various drug delivery systems preparation confirms the importance of these specialized excipients in pharmaceutical application. They represent the choice solution for many oral delivery problems like fluctuating drug plasma levels, low bioavailability, more frequent dose administration etc. So matrix tablets can overcome the above problems of conventional oral drug delivery.

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