ISSN: 2455-2828

Contents lists available at http://www.albertscience.com

ASIO Journal of Drug Delivery (ASIO-JDD)

Volume 6, Issue 1; 2022; 01-08

MATRIX TYPES DRUG DELIVERY SYSTEM FOR SUSTAINED RELEASE: A REVIEW

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ARTICLE INFO

Review Article History

Received: 12th March, 2022
Accepted: 22nd March, 2022

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ABSTRACT

Drug release can be properly maintained using matrix tablets made from an acceptable blend of polymers. Maintaining the drug's efficacy may be aided by maintaining its release. The system is cost-effective since it is built of easily available polymers. These systems are especially beneficial for individuals who require continuous medication delivery over a long length of time. It is an effective technique for medications that are not intrinsically long-lasting and require numerous daily dosing to obtain the intended therapeutic effects; it improves patient compliance as compared to traditional dosage forms. As a result, for medications with a short half-life, a sustained release drug delivery system is chosen in order to keep the drug plasma level in the therapeutic index for a longer length of time. Many new systems are still being developed. However, before launching a new product, the marketability and feasibility of each new formulation must be thoroughly evaluated.

KEYWORDS: Matrix tablet, Sustained Release, *in-vitro* dissolution, polymers.

How to cite the article

Surbhi Sharma, Subas Chandra Dinda, Himanshu Sharma, Matrix types drug delivery system for sustained release: a review, ASIO Journal of Drug Delivery, 2022, 6(1): 01-08.

INTRODUCTION

Drugs are administered with a main aim of treatment of the diseases. Drugs are never administered in their pure form but are converted into a suitable dosage form so that itsonset and intensity of action as well as total duration of action can be checked. Sustained release dosage forms are designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. The basic rationale of sustained release drug delivery system optimizes the biopharmaceutical, pharmacokinetic and Pharmacodynamics properties of a drug in such a way that its utility is maximized, side-effects are reduced and cure/treatment of the disease is achieved [1].

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 can be defined as the oral solid dosage forms in which the drug is homogeneously dispersed or dissolved within the hydrophilic or hydrophobic polymeric matrices. Hypothetically, sustained release dosage form should release the drug by a zero-order mechanism which maintainsdrug plasma level time similar to intravenous infusion. Matrix system is the release system which prolongs and controls the release of the drug, which is dissolved or dispersed. A matrix is definedas a well-mixed composite of one or more drugs with gelling agent i.e., hydrophilic polymers. Introduction of matrix tablet as sustained release has given a new breakthrough for novel drug delivery system in the field of pharmaceutical technology [2].

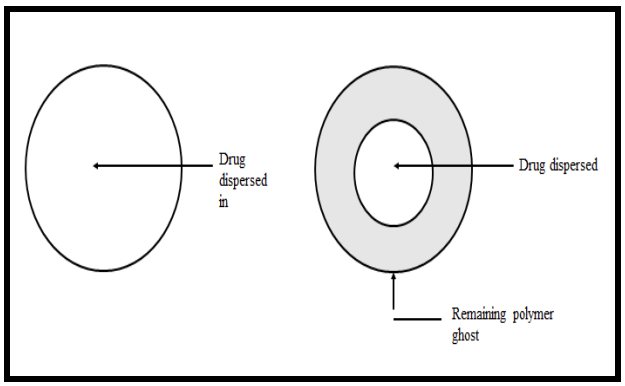

Fig. 1: Release of drug dispersed in an inert matrix system [2]

DOI Link:: 10.2016-21915953/ ; DOI Link :: https://doi-ds.org/doilink/03.2022-65678198/ASIO-JDD/10.2016-21915953/2022/V6I1/920

ADVANTAGES OF SUSTAINED RELEASE MATRIX TABLETS: [3]

1) Improved patient compliance.
2) Reduced drug plasma level fluctuation.
3) Reduction the total dose.
4) Improvement of deficiency in treatment.
5) Reduction the cost of treatment.

DISADVANTAGES OF MATRIX TABLETS:

1) Dose dumping may occur with the faulty formulation.
2) More cost than conventional dosage form formulation.
3) Reduced potential for dose adjustment.
4) Increased potential for first pass metabolism.
5) Poor in vivo and in vitro correlation.

Characteristics of Drug Suitable for sustained Release Tablet: [4]

The ideal physicochemical and pharmacokinetic qualities of medications which can be defined asextended-release tablet are as per the following:

1. Atomic size ought to be beneath of 1000 Dalton.
2. Aqueous solvency ought to be in excess of 0.1 mg/ml for pH 1 to pH 7.8.
3. The partition coefficient ought to be high.
4. Absorption mechanism ought to be diffusion and the general absorbability from all GI fragments discharge ought not to be impacted by pH and catalysts.
5. Drugs ought not to metabolize before absorption it causes less bioavailability.
6. Absolute bioavailability ought to be at least 75% or more.
7. Absorption rate constant (Ka) ought to be higher than discharge rate. Apparent volume of distribution (Vd) ought to be substantial.
8. Total clearance ought not to rely upon dosage.
9. Elimination rate constant are required for design and therapeutic concentration (Css) ought to be low and smaller (Vd).

CLASSIFICATION OF MATRIX TABLETS:

A) On the basis of retardant material used:

This matrix tablets can be divided in to the following types:

1) **Hydrophobic matrices (plastic matrices):**

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) **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. In fact, a matrix is defined as well mixed composite of one or more drugs with a gelling agent (hydrophilic polymer). The polymers used in the preparation of hydrophilic matrices are divided in to three broad groups.

3) **Cellulose derivatives:**

Methylcellulose 400 and 4000 cps, Hydroxyethyl Cellulose, Cellulose Hydroxypropyl methyl Cellulose (HPMC)-25, 100, 4000 and 15000 cps; and Sodium carboxy methyl-cellulose.

4) **Non cellulose natural or semi synthetic polymers:**

Agar-Agar; carbo gum; alignates; maloasses; polysaccharides of mannose and galactose, chitosan and modified starches.

5) **Biodegradable matrices:**

These consist of the polymers which comprised of monomers linked to one another through functional group and have unstable linkage inthe 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 and poly anhydrides.

6) **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 by the use of dilute alkali.

7) **Fat wax matrix tablets:**

The drug can be incorporated into fat wax granules by spray congealing in the air, blend congealing in an aqueous media with or without the aid of surfactant and spray drying techniques. By bulk congealing method, a suspension of drug and melted fat wax is allowed to solidify and is then comminuted for sustainedrelease granulation.

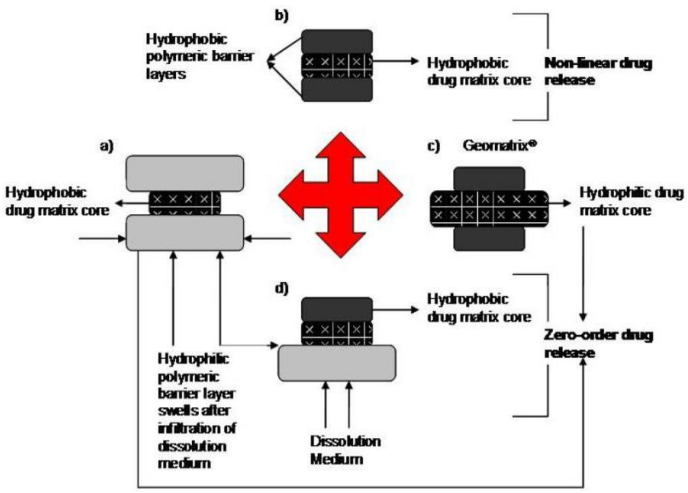

Fig. 2: Possible drug release mechanism from various matrix systems [4]

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B) On the basis of porosity of matrix:

1) **Macro-porous system:**
In such system the diffusion of drug occurs through pores of matrix, which are of size range 0.1 to 1micrometer.this pore size is larger than diffuse molecules size.

2) **Micro-porous system:**
Diffusion in this type of system occurs essentially through pores. For micro porous system, pore size ranges between 50-200A, which is slightlylarger than diffuse molecules size.

3) **Non-porous system:**
Non porous system has no pores and the molecules diffusethrough the network meshes. In this case, only the polymeric phases exist and no pore phase is present.

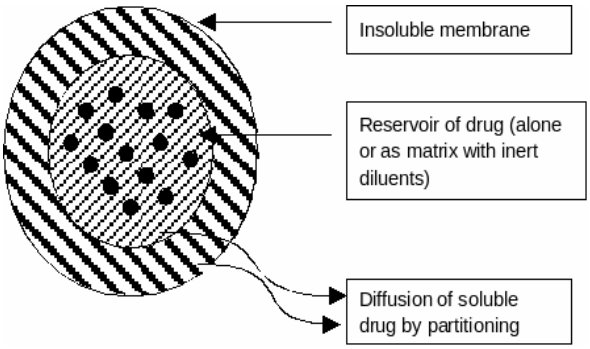

Fig. 3: Diffusion across the Matrix [4]

MATERIALS USED FOR FORMULATION OF MATRIX TABLETS

POLYMERS USED FOR MATRIX FORMULATIONS: [5]

1) **Hydrophilic polymers:** Hydroxyl propyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyl ethyl cellulose (HEC), xanthan gum, sodium alginate, polyethylene oxide and cross linked homopolymers of acrylic acid.

2) **Hydrophobic polymers:** This usually includes waxes and water insoluble polymers in their formulations.

3) **Soluble polymers:** Polyethylene glycol (PEG), polyvinyl alcohol (PVA), polyvinyl pyrrolidine (PVP), hydroxypropyl methyl cellulose (HPMC)

4) **Biodegradable polymers:** Polylactic acid (PLA), polyglycolic acid, polycaprrolactone (PCL), polyanhydrides, polyorthoesters.

5) **Non–biodegradable matrices:** polyethylene vinyl acetate (PVA), poly urethane (PUE), polyvinyl chloride (PVC), cellulose acetate, ethy acetate.

6) **Mucoadhesive polymers:** Polycarbophil, sodium carboxymethyl cellulose, tragacanth, methyl cellulose, pectin.

7) **Natural gums:** Xanthan gums, guar gum, karaya gum, gum arabic, locust from.

OTHER EXCIPIENTS USED IN MATRIX TABLET [6]

1) **Diluents:** Diluents are fillers designed to make up the required bulk of tablets when drugs dosage itself is inadequate to produce this bulk. For example: Talc, calcium carbonate, fructose, dextrose, calcium sulfate and mannitol, etc.

2) **Binder and adhesives:** Acacia mucilage, Alginic acid, carbomer, Guar gum, Methyl cellulose and Gelatin.

3) **Lubricants and glidants:** Lubricants- calcium stearate, fumaric acid, starch, talc, stearic acid. Glidants-calcium silicate, magnesium carbonate, silicon dioxide, magnesiumoxide and talc etc.

4) **Colors, flavors and sweeteners:** The use of colors is used to provide attractive appearance for off- color drugs. Flavors and sweeteners are usually limited to chewable tablets or other tablets intended to dissolve in mouth.

Table 1: Combination of few drugs and category of polymers used in matrix tabletformulation [7]

Drug	Polymer	Drug	Polymers
Zidovudine	HPMC-K4M, Carbopol-934, EC	**Furosemide**	**Guar gum, pectin, Xanthan gum**
Ibuprofen	EC, CAP	**Aceclofenac**	**HPMC- K4M, K15M, K100M, E15, EC**
Enalpril meleate	HPMC-K100M,HPMC-K4M, Sod. CMC	**Aspirin**	**EC, Eudragit-RS100,S100**
Metformin HCL	HPMC-K100M, EC	**Diclofenac Na**	**EC, HPMC**
Indomethacin	EC, HPMC	**Diltiazem**	**Karaya gum, Locust bean gum, Sod, CMC**
Metoclopramide	HPMC, CMC, EC,SSG	**Ondansetron**	**HPMC-K100M,HPMC-K4M, Tragacanth, HPMC-K15M**
Losartan potassium	HPMC-K100M,HPMC-K4M, Eudragit-RSOP	**Phenytoin Na**	**Acacia, Guar gum, Xanthan gum**
Clorpheniraine maleate	Xanthan gum,Chitoson	**Ranitidine HCL**	**Chitoson,Carbopol-940**
Tramadol	Karaya gum,HPMC-K4M	**Theophyline**	**HPMC-K100M, Carbopol-934, HPMC-K4M, EC**

DOI Link:: 10.2016-21915953/ ; DOI Link :: https://doi-ds.org/doilink/03.2022-65678198/ASIO-JDD/10.2016-21915953/2022/V6I1/920

DESIGN AND FORMULATION OF ORAL SUATAINED RELEASE MATRIXTYPEDRUG DELIVERY SYSTEM:

The oral route of administration is the most preferred route due to flexibility in dosage form, design and patient compliance. But here one has to take into consideration, the various pH that the dosageform would encounter during its transit, the gastrointestinal motility, the enzyme system and its influence on the drug and the dosage form 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. Derivationof the mathematical model to describe this system involves the following assumptions [8].

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 throughthe matrix;

c) The bathing solution provides sink conditions at all times. The release behavior for the system can be mathematically described by the following equation: **=**

Co. Dh - Cs/2---------- (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 drugCo = Total amount of drug in a unit volume of matrix
Cs = Saturated concentration of the drug within the matrix.
Additionally, according to diffusion theory:

dM = (Dm. Cs / h). Dt---------- (2)

Where, dm = 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 = [Cs. Dm. (2Co−Cs). t] ½— (3)

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

M = [2Cs. Dm. Co. t] ½ ----(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 = [Ds.Ca. p/T. (2Co – p. Ca) t] ½ ----(5)

Where, p = Porosity of the matrixt = Tortuosity
Ca = solubility of the drug in the release mediumDs = Diffusion coefficient in the release medium.
T = Diffusion path length for pseudo steady state, the equation can be written as:

M = [2D. Ca. Co (p/T) t] ½---------- (6)

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

p = pa + Ca/ ρ + Cex / ρex ---------- (7)

Where, p = Porosityρ = Drug density
pa = Porosity due to air pockets in the matrix
ρex = Density of the water-soluble excipients
Cex = Concentration of water-soluble excipients for the purpose of data treatment, equation 7 canbe reduced to:

M = k. t ½---------- (8)

Where k is a constant, so that the amount of drug released versus the square root of time will belinear, if the release of drug from matrix is diffusion-controlled.

Higuchi has derived the appropriate equation for drug release for this system

Q = Dε/ T [2 A –εCs] Cst½ -------(9)

Where;
Q = Weight in grams of drug released per unit area of surface at time t.D = Diffusion coefficient of drug in the release medium.
ε = Porosity of the matrix.
Cs = Solubility of drug in release medium.T= Tortuosity of the matrix.
A = Concentration of drug in the tablet, as gm/ ml.

Description: Homogenous dispersion of solid drug in a polymer mixture.

Advantages: Easier to produce than reservoir or encapsulated devices, can deliver high molecular weight compounds.

Disadvantages: Cannot provide zero order release, removal of remaining matrix is necessary for implanted system. Diffusional mechanism is the system where a partially soluble membrane encloses a drug core. Dissolution of part of membrane allows for diffusion of the constrained drugthrough pores in the polymer coat.
The release rate can be given by following equation.

Release rate = AD / L = [C1- C2] -------(10)

Where;
A = Area.
D = Diffusion coefficient.
C1 = Drug concentration in the core.
C2 = Drug concentration in the surrounding medium.L = Diffusional path length.
Thus, diffusion sustained products are based on two approaches the first approach entails placementof the drug in an insoluble matrix of some sort. The eluting medium

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penetrates the matrix and drugdiffuses out of the matrix to the surrounding pool for ultimate absorption. The second approach involves enclosing the drug particle with a polymer coat.

2. Dissolution Sustained Systems:

A drug with a slow dissolution rate is inherently sustained and for those drugs with high water solubility, one can decrease dissolution through appropriate salt or derivative formation. These systems are most commonly employed in the production of enteric coated dosage forms. To protect the stomach from the effects of drugs such as Aspirin, a coating that dissolves in natural or alkalinemedia is used. This inhibits release of drug from the device until it reaches the higher pH of the intestine. In most cases, enteric coated dosage forms are not truly sustaining in nature, but serve as a useful function in directing release of the drug to a special site.

i) Reservoir Type: Drug isolated with a given thickness coating, which is slowly dissolved in the contents of gastrointestinal tract. By alternating layers of drug with the rate controlling coats as shown in figure, a pulsed delivery can be achieved. If the outer layer is quickly releasing bolusdose of the drug, initial levels of the drug in the body can be quickly established with pulsed intervals. Although this is not a true sustained release system, the biological effects can be similar.An alternative method is to administer the drug as group of beads that have coating of different thickness. The maintenance of drug levels at late times will be achieved from those with thicker coating [9].

ii) Matrix Type: These are common type of dissolution sustained dosage form. It can be eithera drug impregnated sphere or a drug impregnated tablet, which will be subjected to slow erosion. Two types of dissolution sustained pulsed delivery systems

- ✓ Single bead type device with alternating drug and rate-controlling layer.
- ✓ Beads containing drug with differing thickness of dissolving coats.

Amongst sustained release formulations, hydrophilic matrix technology is the most widely used drug delivery system due to following advantages.

- ✓ Provide desired release profiles for a wide therapeutic drug category, dose andsolubility.
- ✓ Simple and cost-effective manufacturing using existing tablets unit operation equipment.
- ✓ Broad regulatory and patient acceptance.
- ✓ Ease of drug release modulation through level and choice of polymeric systems and function coatings.

3. Methods Using Ion Exchange

It is based on the formation of drug resin complex formed when anionic solution is kept in contact with ionic resins. The drug from these complexes gets exchanged in gastrointestinal tract and released with excess of Na+ and Cl- present in gastrointestinal tract.

Anion Exchangers:

Resin+ - Drug- + Cl- goes to Resin+- Cl-+ Drug-

Cation Exchangers:

Resin-- Drug+ + Na+ goes to Resin- - Na+ + Drug+

These systems generally utilize resin compounds of water insoluble cross-linked polymer. They contain salt forming functional group in repeating positions on the polymer chain. The release ratecan be further sustained by coating the drug resin complex by microencapsulation process.

4. Methods Using Osmotic Pressure

A semi permeable membrane is placed around a tablet, particle or drug solution that allows transport of water into the tablet with eventual pumping of drug solution out of the tablet through a small delivery aperture in tablet coating.

Two types of osmotically sustained systems areType A contains an osmotic core with drug.

Type B contains the drug in flexible bag with osmotic core surrounding.

5. pH– Independent Formulations

The gastrointestinal tract presents some unusual features forth oral route of drug administration with relatively brief transit time through the gastrointestinal tract. Since most drugs are either weakacids or weak bases, the release from sustained release formulations is pH dependent. A buffered sustained release formulation is prepared by mixing a basic or acidic drug with one or more buffering agent, granulating with appropriate pharmaceutical excipients and coating with gastrointestinal fluid permeable film forming polymer. When gastrointestinal fluid permeates through the membrane, the buffering agents adjust the fluid inside to suitable constant pH thereby rendering a constant rate of drugrelease [10].

METHODS OF PREPARATION:

1) **Direct compression:** In this method, finely powdered materials are compressed directly without changing the physical and chemical properties of the drug.
2) **Wet granulation:** In this method weighed quantities of drug and polymer are mixed with sufficient volume of the granulating agent. After enough cohesiveness was obtained,the mass is sieved and dried at 40°c and kept in a desiccator. Lubricants and glidants are added the tablets are compressed using a tablet compression machine.
3) **Melt granulation:** In melt granulation, meltable substance act as liquid binding agent and hence does not require the use of organic solvent. This substance can be added in the molten from over the substrate, which is then heated above the substrate, which is then heated above its melting point. Various lipophilic binders such as glyceryl palmitostarate are used in melt granulation technique.

CRITERIA TO BE MET BY DRUG PROPOSED TO BE FORMULATED INSUSTAINED RELEASE DOSAGE FORMS:

There are some physicochemical parameters of the drug selection to be formulated in sustained release dosage form which mainly includes the knowledge on the absorption mechanism of the drug form the gastro intestinal (G.I) tract, its general absorbability, the drug's molecular weight, solubility at different pH and apparent partition coefficient as shown in Table 2.

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Table 2: Physicochemical parameters

Parameter	Preferred value
Molecular weight	<1000 Daltons
Solubility	>0.1 mg/ml for pH 1 to pH 7.8
Apparent partition coefficient	High
General absorbability	From all GI segments
Release	Should not be influenced by pH and Enzymes
Absorption mechanism	Diffusion

Similarly, there are some pharmacokinetic parameters for drug selection which includes drug's elimination half-life, total clearance, absolute bioavailability, possible first pass effect, and the desired steady concentration for peak and through as shown in Table 3.

Table 3: Pharmacokinetic parameters for drug selection

Parameter	Comment
Elimination half life	Preferably between 2to8hr
Total clearance	Should not be dose dependent
Elimination rate constant	Required for design
Apparent volume of distribution (Vd)	The larger Vd and MEC, the larger will be the required dose size
Absolute bioavailability	Should be 75% or more
Intrinsic absorption rate	Must be greater than release rate
Therapeutic concentration Css	The lower Css and smaller vd, the loss among of drug required
Toxic concentration	Apart the values of MTC and MEC, safer the dosage form. Also suitable for drugs with veryshort half life

EFFECT OF VARIOUS PARAMETERS ON DRUG RELEASES: [11]

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).

1. 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.

2. 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 includes absorption/adsorption of water in more accessible places, rupture of polymer-polymer linking with the simultaneous forming of water-polymer linking, separation of polymeric chains, swelling and finally dispersion of polymeric chain in dissolution medium.

3. Polymer diffusivity: The diffusion of small molecules in polymer structure is energy activated process in which the diffuse molecules move to a successive series of equilibrium position whena sufficient amount of energy of activation for diffusion Ed has been acquired by the diffusion 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-

- **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.
- **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.

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

5. 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

7. 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

8. Effect of diluents: The effect of diluent or filler depends upon the nature of diluent. Water soluble diluents like lactose cause marked increase in drug release rate and release mechanism is also shifted towards Fick's diffusion; while insoluble diluents like Di calcium phosphate reduce the Fick's 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

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drugrelease rate.

9. Molecular weight and size: Drugs with a molecular weight of >5000 Dalton are through to have poor diffusion through the hydrophilic matrices due to the constrain imposed by the aqueousgel structure.

10. Metabolism: The metabolic conversion to a drug is to be considered before converting into another form. Since as long as the location, rate, and extent of metabolism are known a successful sustain release product can be developed.

DRUG RELEASE FROM MATRIX

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 rateof dissolution of drug particles within the matrix must be much faster than the diffusion rate of dissolved drug leaving the matrix.

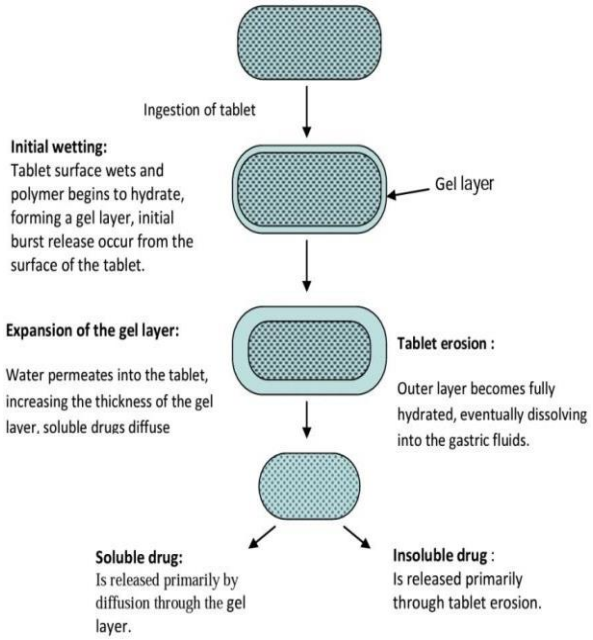

Fig. 4: Drug release from hydrophilic matrix tablet advantages [11]

Derivation of the mathematical model to describe this system involves the following assumptions. A pseudo-steady state is maintained throughout drug release, the diameter of the drug particles is fewer than the average distance of drug diffusion through the matrix, the diffusion constant of drug in the matrix remains constant (no vary occurs in the characteristics of the polymer matrix.

In a hydrophilic matrix, there are two opposite mechanisms involved in the drug release: Fick's diffusion release and relaxation release. Diffusion is not the only way by which a drug is released from the matrix; the erosion of the matrix following polymer relaxation contributes to the overallrelease. The relative contribution of every component to the total release is primarily dependent relative on the properties of a given drug. For example, the release of a sparingly soluble drug from hydrophilic matrices involves the immediate absorption of water and activity of drug via a swelling-controlled diffusion mechanism. When water penetrates into a glassy polymeric compound matrix, the polymer swells and its glass transition temperature is lowered. At the constant time, the dissolved drug diffuses through this swollen rubbery region into the external releasing medium. This type of diffusion and swelling does not usually follow a Fickian diffusion mechanism. The semi-empirical equation to explain drug release behavior from hydrophilic matrix systems.

Q = k tn

Where,

Q = fraction of drug released in time.

k = rate constant incorporating characteristics of the macromolecular network system and the drug n = the diffusional exponent. It has been shown that the value of n is indicative of the drug releasemechanism.

EVALUATION OF SUSTAINED RELEASE MATRIXTABLETS:

Before marketing a sustained release product, it must to assure the strength, safety, stability and reliability of a product by forming in–vitro and in–vivo analysis and correlation between the two. Various parameters are available for evaluation of sustained release matrix 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 thickness of tablets was determined using micrometer screw gauge (4).
5. **Content uniformity:** Using UV visible spectrophotometer can find the amount of the drug using the calibration curve.
6. **Kinetic studies:**

- ***IN-VITRO* method:** Beaker method, rotating disc method, rotating bottle method, rotatingbasket method, dialysis method, US dissolution method and stationary basket method.
- ***IN-VIVO* method:** Once in vitro profile is achieved, it becomes necessary to conduct invivo evaluation and establish in vitro in vivo correlation.

The various evaluation methods are:

- ✓ **Clinical response**
- ✓ **Blood level data**
- ✓ **Urinary excretion studies**
- ✓ **Nutritional studies**
- ✓ **Toxicity studies**

BIOAVAILABILITY TESTING:

Bioavailability is generally defined as the rate and extent of absorption of unchanged drug from its site of application to the general circulation. Bioavailability is defined in terms of a specific drug moiety, usually active therapeutic entity, which may be the unchanged drug or as with pro-drug, for instance, a metabolite. In contrast, the term "absorption" often refers to net transport of drug related

DOI Link:: 10.2016-21915953/ ; DOI Link :: https://doi-ds.org/doilink/03.2022-65678198/ASIO-JDD/10.2016-21915953/2022/V6I1/920

mass from its site of application into the body. Pharmaceutical optimization of the dosage form may be warranted to improve absorption characteristics of the drug and thereby also its bioavailability. Bioavailability studies are ordinarily single dose comparisons of tested drug product in normal adults in a fasting state. While single dose studies are usually sufficient to establish the validity of sustained release dosage form design; multiple dose studies are required to establish optimum dosing regimen. When there is excessive subject-to subject variation or when the observed blood levels after a single dose are too low to be measured accurately [12].

Table 4: COMMERCIAL APPLICATIONS: [12]

DRUGS USED	CATEGORY
Zidovudine	**Anti-viral**
Domperidone	**Anti-emetic**
Ibuprofen	**Anti-inflammatory**
Metformin HCL	**Anti-diabetic**
Propranolol HCL	**Beta adrenergic blocker**
Frusemide	**Anti-diuretics**
Aceclofenac	**Anti-inflammatory**
Aspirin	**Anti-inflammatory**
Enalpril maleate	**ACE inhibitor**
Indomethacin	**Anti-inflammatory**
Losartan potassium	**Anti-hypertensive**
Naproxen	**Morphine antagonist**
Ondansetron	**Anti-hypertensive**
Phenytoin Na	**Anti-epileptic**
Ranitidine HCL	**H2 Antagonist**
Theophylline	**Respiratory depressant**
Verapamil	**Ca+2 channel blocker**
Amlodipine	**Anti-arrythmatic**

CONCLUSION

From the discussion, it can be concluded that matrix tablets, developed by using a rational combination of polymers can successfully applied to sustain the release of the drug. Sustaining the release of the drug may be helpful in increasing the efficiency of the drug. The system is economic since these are developed by using the commonly available polymers. These systems are especially useful in case of patient who needs a constant delivery of drug for a longer period of time. It is effective tool for drugs that are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic effects; when compared to conventional dosage form it provide improved patient compliance. Hence, sustained release drug delivery system is the preferred form for the drugs having short life, so as to maintain the drug plasma level in therapeutic index for prolonged period of time. Many new systems are still emerging. But the marketability and feasibility of each new formulation has to be assessed carefully before launching new product.

REFERENCES

1. Jaimini M, kothari AH. Sustained release matrix type drug delivery system: a review. World journal of pharmacy and pharmaceutical science. 2012; 5; 1(3): 934-60.
2. Karvekarmayur, khan bashir Arshad. A brief review on sustained release matrix type drug delivery system. Journal of pharmaceutical Research. 2017; 282-289.
3. Bhargava Ankit, Rathore R.P.S, Tanwar Y.S, Gupta s, Bhaduka G, Oral sustained release dosage from: An opportunity to prolong the release of drug. International journal of advanced research in pharmaceutical & Bio science. 2013; 3(1): 7-14.
4. Nisargishah, chitanoza, Shitaltrivedi, Nihar shah, sheeraj shah, Review on sustained release matrix tablets: An Approach to prolong the release of drug. Journal of pharmaceutical sciences and bioscientific research (JPSBR). 2015; 315-321.
5. Dixit N, Maurya SD, P.S. Sagar B. sustained release drug delivery system. India journal of research in pharmacy and biotechnology. 2013; (1): 305-10.
6. Higuchi T. Mechanism of sustained action medication: theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J. pharma.Sci. 1961; 52(1): 1145-59.
7. AlhalmiAbdulsalam, Altowairi Marwan, Saeed Omer, AlzubaidiNafaa, Almoiliqy Marwan, AbdulmalikWatheeq. Sustained release matrix system: on overview. World Journal of pharmacy. 2018;1470-1485.
8. Sharma Ashish and Bhatt Vikas, Sustained release matrix type drug delivery system: A review. World journal of pharmacy and pharmaceutical sciences. 2015; 1002-1022.
9. Agarwal Prakhar, Akhtar Semimul, A Comprehensive Review on sustained Release Matrix Tablets; A promising Dosage Form, Department of pharmacy, universal journal of pharmaceutical research. 2018; 53-58.
10. Mandal Nita, The Role of Matrix Tablet in Drug Delivery System. International of applied pharmaceutics. 2018; 1-6
11. Patel Harnish, Dhrupesh R. Panchal, BrahmbhattTushar, SutharMayur. Matrix type drug delivery system: A review. Journal of pharmaceutical science and Bioscientific Research. 2011; 143-151.
12. Lachman L, Liberman HA, "The theory and practice of industrial pharmacy", CBS publishers & Distributors, 4th edition 2013; 459-466.

DOI Link:: 10.2016-21915953/ ; DOI Link :: https://doi-ds.org/doilink/03.2022-65678198/ASIO-JDD/10.2016-21915953/2022/V6I1/920