



A Review on : Matrix Drug Delivery System

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ABSTRACT:

The popular and convenient drug administration route is oral. For both traditional and cutting-edge medication delivery systems, oral route of administration has been used. For medications that are given orally but have a high dose frequency and short half life, an oral controlled release drug delivery device becomes a very interesting method. Matrix tablets are an important tool in the development of oral controlled release dosage forms. This review focuses on the different types of matrix systems depending on the polymer employed and the porosity of the matrix system, such as hydrophilic, hydrophobic, and hydrophobic matrix systems. The goal of a sustained or controlled drug delivery system is to reduce the frequency of dosing or increase the efficacy of a drug by localising it at the site of action, lowering the dose required, providing continuous drug delivery, reducing the incidence of adverse effects, and maintaining drug concentration in the system. The goal of this review is to have a thorough understanding of the matrix drug delivery system.

Keywords: Matrix tablet, hydrophilic polymer, controlled release.

Introduction

Oral Drug Delivery System

The oral route is the most commonly used method of drug management. The oral cavity is also the oldest and appropriate way to manage medical agents due to low treatment costs and convenience. Management leads to a higher level of patient obedience. About 50% of drug products are available in the market they are treated orally and historically, oral drug administration has been a major route for drug delivery. Tablets are the most common as well as widely used volume form. [1] Oral method is the simplest form of drug to manage. To date many oral dosage forms are still available designed to improve patient compliance. Drugs with a small fraction of life are excreted from the body in a short time. Such drugs are necessary to be it is often used to determine the required plasma concentration levels. The increase in dose frequency may decrease patient compliance. This difficulty can be avoided by making drugs as a continuous release of the matrix type drug delivery programs. [2]

The oral route is highly appreciated and comprehensive route of drug management. The route of oral administration has been used for both conventional and novel drug delivery systems. In the present case, the measure form of continuous release fails to use standard volume form. The continuous release tablet provides the same drug release for a long time. Controlled output volume form includes a wide range of long action composition that provides for their continuous release of an active ingredient in a predetermined amount and time. Ongoing or controlled drug delivery program to reduce frequency of dosing or increasing efficiency of the drug by making a place in the action area, reducing the dose needed, to provide continuous drug delivery, reduction in incidence of adverse effects and drug retention to focus on the system. [3]

Matrix Drug Delivery System

These are the kind of controlled drug delivery systems releasing the drug in a continuous way for both of them dispersion is controlled and distribution is controlled methods. Controlling drug release, which they have different melting points, the drug is dispersed in an inflamed hydrophilic substance, in an insoluble hydrophobic solid matrix that does not swell building materials or plastic materials. [4] Introducing the matrix tablet as a continuous release (SR) provided a new approach to drug delivery system in the field of Pharmaceutical technology. It does not include complex production processes such as coverage and pelletization during drug production and release the rate from the volume form is largely controlled by the type and part of the polymer used in the preparation. Hydrophilic polymer matrix is widely used to form an SR volume form. [5] Matrix systems are widely used for this purpose continuous release. It is an extension program and controls the release of the dispersed drug or they are scattered. In fact, the matrix is defined as well-mixed a combination of one or more drugs with a gelling agent i.e. hydrophilic polymers. In the form of continuous release effective treatment can be achieved in the system cycle for a long time, thus achieving better patient compliance. [6]

Advantage of matrix drug delivery system

1. Reduce negative local and systemic effects.
2. Flexible, efficient and low cost
3. Reduce toxicity by reducing drug absorption.
4. Reduce drug overdose by chronic dose.

Disadvantage of matrix drug delivery system

1. Not all drugs can be combined with a given polymeric matrix.
2. The remaining matrix must be removed after the drug is released.
3. Finding a zero order is difficult.
4. Drug release rates vary by square root of time.

Matrix tablet

One of the cheapest ways to the construction of controlled release volume forms involves direct compression of a drug compound, retardant materials and supplements to build a tablet where the drug is embedded in the retardant matrix. On the other hand a combination of drugs and retardant may be granulated before pressing. [7]

Classification of matrix Tablet

Lipid matrix system: These matrices are fixed by lipid wax and are related building materials. In this program the active combination is contained in a time-consuming hydrophobic matrix drug release. Exfoliation depends on the water content to melt the track agent, leaking out compact, so form a matrix with tortuous holes capillaries. The active agent dissolves in water medium and, in the form of water filled capillaries, disperses outside the matrix.

Hydrophilic matrices: These transfer systems are also called swellable -soluble matrices. The systems are prone to inflammation, followed by gel formation, erosion and dispersion water media. Components of hydrophilic colloid swell to form a layer of liquid matrix when in contact with water. This controls the further distribution of water in the middle matrix. Hydrated drug distribution matrix layer controls the rate of release. Outside the hydrated matrix layer will erode as it transforms more clean. The rate of erosion depends on the condition of colloid.

Polymer gastrointestinal : The medicine in this approach is encased in an inert polymer that is not soluble in gastrointestinal fluids. Drug molecules in aqueous solution diffusing via a network of capillaries produced between compressed polymer particles determine the release rate. Changes in the porosity and tortuosity of an inert matrix can affect the pace at which a medication is released. Drug release will be heavily influenced by pore-forming hydrophilic salts or solutes. [8]

Biodegradable matrix system : The polymeric materials utilised in this sort of matrix system are monomers linked to each other by functional groups with instable functionality. Polymeric materials are broken down into oligomers and monomers using either biological enzymes produced by the surrounding tissues or non-enzymatic mechanisms. Proteins, polysaccharides, aliphatic polyesters, and polyanhydrides are examples of natural polymers used in this matrix base. Synthetic polymers include polyanhydrides.

Hydrophobic Matrices (Plastic matrices): The medicine is combined with an inert or hydrophobic polymer and crushed into a tablet in this method of generating sustained release from an oral dosage form. The dissolving medication diffuses through a network of channels between compressed polymer particles, resulting in sustained release. Polyethylene, polyvinyl chloride, ethyl cellulose, and acrylate polymers and copolymers have all been employed as hydrophobic matrices. In these formulations, liquid penetratioPhaeophyceae into the matrix is the rate-controlling step. Diffusion is a proposed mechanism for drug release in these types of tablets. [9]

Mineral Matrices [10]: These are made up of polymers derived from several seaweed species. Alginic acid, for example, is a hydrophilic carbohydrate produced by dilute alkali from brown seaweed species. Based on the Porosity of the Matrix: The Matrix system can and are classified according to their porosity as well as a result, Macro has holes; Micro porous as well Waterless systems can be seen.

1. Macro Porous Systems

In such systems the distribution of the drug occurs matrix holes, which are 0.1 to 1 μm in size. This pore size is greater than particle size separated.

2. Micro Porous System

Distribution on this type of system occurs basically through the holes. In micro porous systems, pore size distance between 50 - 200 \AA , slightly larger than the size of the dividing molecules.

3. Non-porous system

Non-porous systems have no pores and molecules we distributed them through network matches. In this case, only the polymeric phase is present and no pore phase is present.

Polymers Used In Matrix Tablet

1)Hydrogels

Cross-linked Polyvinyl Pyrrolidone (PVP)
Polyethylene oxide (PEO), Polyacrylamide (PA)
Cross-linked Polyvinyl Alcohol (PVA)
Poly Hydroxy Ethyle Methylacrylate (PHEMA)

2)Soluble polymer

Hydroxypropyl methyl cellulose (HPMC)
Polyvinyl Pyrrolidone (PVP)
Polyvinyl Alcohol (PVA)
Polyethylene Glycol (PEG)

3)Biodegradable polymer

Polycaprolactone (PCL)
Polyglycolic acid (PGA)
Polyanhydrides
Polylactic acid (PLA)
Polyorthoesters.[11]

4)Non-biodegradable polymer

Ethyl cellulose (EC)
Cellulose acetate (CA)
Polyvinyl chloride (PVC)
Polyether urethane (PEU)
Polyethylene vinyl acetate (PVA)
Polydimethylsiloxane (PDS)

5)Mucoadhesive polymer

Tragacanth
Polyacrylic acid
Sodium carboxymethyl cellulose
Polycarbophil
Methyl cellulose, Pectin.[12]

6)Natural gum

Karaya gum
Guar gum
Xanthan gum
Locust bean gum.[13]

Method of Preparation of Matrix Tablet

A. Wet Granulation Technique[9]

Milling and mixing of drug, polymer and excipients.
Preparation of binder solution.
Wet massing by addition of binder solution or granulating solvent.
Screening of wet mass.
Drying of the wet granules.
Screening of dry granules.
Blending with lubricant and disintegrant to produce “running powder”
Compression of tablet.

B. Dry Granulation Technique[14]

Milling and mixing of drug, polymer and excipients.
Compression into slugs or roll compaction.

Milling and screening of slugs and compacted powder.

Mixing with lubricant and disintegrant

Compression of tablet

C. Sintering technique[10]

The joining of neighbouring particle surfaces in a mass of powder, or in a compact, by the application of heat is referred to as sintering. Sintering is a process that involves heating a compact to a temperature below the melting point of the solid constituents in a controlled environment. The effects of sintering on the hardness and disintegration time of tablets held at high temperatures were studied. For the stabilisation and slowing of drug release, the sintering method has been used in the manufacture of sustained release matrix tablets.

MECHANISM OF DRUG RELEASE FROM MATRIX TABLETS[14]

Diffusion controlled

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.[10]

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. Derivation of the mathematical model to describe this system involves the following assumptions.[15]:

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

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

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_o = 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:

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

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

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

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.

[16,17]

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

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

Where,

p = Porosity of the matrix

t = Tortuosity.

Controlled drug delivery systems:

Controlled drug delivery systems have been created that can manage the pace of drug administration, maintain therapeutic activity for longer periods of time, and/or target drug delivery to a specific tissue. [18] Controlled drug delivery or modified drug delivery systems are categorised into four types for ease of use. 1) A postponed release 2) Consistent release 3) Targeting by location 4) Aiming at specific receptors Controlled delivery is defined as:[19]

- 1) Maintaining a reasonably steady, effective drug level in the body while minimising undesired side effects at a predetermined rate.
- 2) Drug delivery to

a specific target cell type via carriers or chemical compounds. 3) Develop a drug delivery system that is physiologically/therapeutically based.

Advantage of controlled drug delivery system [20]

- 1) Prevent issues with patient compliance.
- 2) Use a less amount of overall medication Minimize or eliminate side effects in the immediate area. Reduce, if not eliminate, systemic adverse effects. Chronic use results in reduced potentiation or a decline in pharmacological action. Chronic dosing helps to keep drug buildup to a minimum.
- 3) Increased therapeutic efficacy Improves the speed with which a problem is cured or managed. Improves condition control, i.e., medication level volatility is decreased. Some medications' bioavailability is increased. Sustained-release aspirin, for example, is used in the morning to relieve pain. Before going to bed, take a dose of arthritis medication.

Disadvantage of controlled drug delivery system

- 1) In the event of toxicity, poisoning, or hypersensitivity reactions, retrieving the medicine is challenging.
- 2) There is a need for more patient education and counselling.
- 3) Issues with stability.
- 4) The price has gone up.
- 5) More quicker tolerance and counselling development.

Factor affecting the design and performance of controlled drug delivery [18]

1. Drug properties

- Partition coefficient
- Drug stability
- Protein binding
- Molecular size and
- Diffusivity.

2. Biological properties

- Absorption
- Metabolism
- Elimination and
- biological half life
- Dose size
- Route of administration
- Target sites
- Acute or chronic therapy
- Disease condition

Mechanism of controlled drug release system

1. Diffusion Controlled System:

The diffusion process essentially depicts the migration of drug molecules from a higher concentration region to a lower concentration region. Fick's law describes the flow of the drug J (in amount / area -time) across a membrane in the direction of decreasing concentration.

$$-D \frac{dc}{dx} = J$$

Where D is the diffusion coefficient in area divided by time.

dc/dx denotes the change in concentration 'c' as a function of distance 'x'.

The release rate of a medicine is determined by its diffusion through an inert, water-insoluble membrane barrier in diffusion systems. Diffusion devices are divided into two categories.

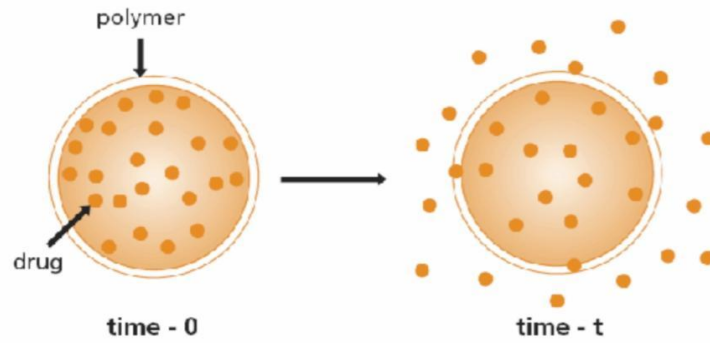


Fig 1: Schematic Representation of Reservoir

Reservoir of type : A water-insoluble polymeric substance encases a drug core in the system, which regulates the pace of release. The drug will partition into the membrane and exchange with the fluid in the vicinity of the particle or tablet. More medication will enter the polymer, diffuse to the periphery, and exchange with the media. Ethyl cellulose and polyvinyl acetate are two polymers typically employed in these devices. [21]

Diffusion Controlled Drug Delivery Device : The level of the extracted drug (dm / dt) can be calculated using the following number

$$dm / dt = ADK \Delta C / L$$

Where, A = Location,

D = Diffusion coefficient,

K = Partition coefficient of drug between drug and gastrointestinal tract,

L = Length of one-way distribution

ΔC = Concentration difference everywhere membrane.

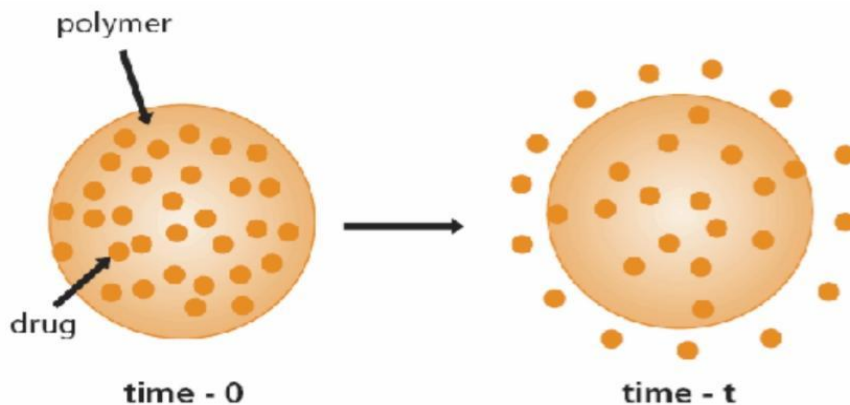


Fig 2: Schematic Representation of Monolithic (matrix) Diffusion Controlled Drug Delivery Device

Matrix type : Solid drug is dispersed in the same way in an insoluble matrix and drug release rate depending on the rate of drug distribution and not on the level of solid finish.

Dissolution controlled system : Controlling the dissolving rate of drugs with a high water solubility and dissolution rate is difficult. Slowing the dissolving rate of a medication in the GI medium, incorporating the drug in an insoluble polymer, and coating drug particles or granules with polymeric materials of varied thickness can all be used to achieve dissolution-controlled release. Diffusion over the aqueous boundary layer is the rate limiting stage in drug dissolution. The medication's solubility provides a source of energy for drug release, which the stagnant-fluid diffusional barrier layer counteracts. The rate of dissolution (dm/dt) can be approximated as

$$dm/dt = ADS/h,$$

where S represents the drug's aqueous solubility.

A = Dissolving particle or tablet surface area.

D = diffusivity of the drug

h = Boundary layer thickness.

Conclusion : As a result of the above explanation, it is easy to deduce that controlled-release formulations aid in enhancing dose efficiency while also improving patient compatibility. Matrix tablets, which release drugs in a regulated manner, can be successfully prepared using matrix forming polymers. Preparatory procedures make it simple to tailor release kinetics to specific delivery requirements. The usefulness of matrix forming polymers in the production of diverse drug delivery systems underpins the significance of these specialised excipients in pharmaceutical applications.

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