Concise Review on modified Release Drug Products of Matrix Tabltes As Drug Delivery System

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Abstract- *Oral route of drug delivery is the most preferred method among the available routes of drug administration. However, the traditional conventional or immediate oral dosage form especially tablets, capsules have a few drawbacks such as rapid rate of drug absorption and onset of accompanying pharmacodynamics effects results in rapid loss in the desired therapeutic activity or poor patient compliance that could be fixed and altered by using current modified release drug products. A regulated and sustained drug delivery system prolongs the duration of action by slowing the drug's release rate and assisting in maintaining a consistent plasma drug concentration, which eliminates poor patient compliance, repeated dosages, and see-saw oscillations after administration into the body. In that matrix tablets, a crucial tool among the numerous formulation options of modified release tablets. A number of hydrophilic or hydrophobic polymers can be used to make matrix tablets using either the direct compression or the wet granulation technique. Rate and extent are the main factor that controls how quickly drugs are released from the matrix tablets. The primary goal of this review is to provide comprehensive understanding of modified release drug product of matrix tablets and its benefits, criteria for drug selection and its formulations details.*

Keywords- drug delivery system,oral route, sustained release, matrix system, polymer.

I. INTRODUCTION

A wide variety of methods used to introduce medicinal substances into the body of an individual and it should be achieved by using a suitable drug delivery system. Drugs as such in their pure form not possible to be administered due to its inherent physicochemical properties, instead a suitable formulation is to be developed with changes on its onset, intensity, and overall duration of the action. (1)Typical dosage forms include solid dosage forms, liquids dosage forms, and topical dosage forms are used to achieve above characteristics. In that all above dosage forms, solid dosage form such as tablets are the most practical and preferred drug delivery system because of lower patient non-compliance, wide flexibility in drug design and development, non-invasiveness, less cost and more affordability in production.. In 1843, the first tablets were developed using a hand operating machine with different size and shape. [2] Different types of tablets includes uncoated,sugar coated, film coated, enteric coated, dispersible, effervescent, chewable, sublingual, buccal and modified release tablets are developed depending on the physio-chemical properties of active substances and excipients.[3] To guarantee the therapeutic concentration of the drug in the body two requirements are to be met that the rate at which the drug is released from dosage form should be equal to the rate of drug elimination at the required steady-state concentration. Various key phrases such as Delayed release, Sustained release, Controlled release, prolonged release, Site-specific release, Receptor release are used to achieve the above properties. Hence, in this paper we have presented the comprehensive details of various modified release product details with special attention on matrix type of tablets. [4]

1. Delayed release system: System that releases a distinct portion of a drugs from its dosage form with certain time lag after administration as well as with control over the drug where it is to be released or targeted is known as delayed release system. Some colon and intestine specific (enteric-coated tablets), repeat-action tablets and capsules(An immediate release dose after an administration, an equivalent to conventional single dose for attaining therapeutic concentration with certain time lag for another dose may be second or third) are developed and released its drug contents in programmed manner to treat site specific diseases is more beneficial for patient than a traditional conventional dosage forms. Suffix DR is used to identify this type of dosage form and valproate is an example of drug used.

2. Sustained release system: Sustains the rate of drug release over a long period of time into the patient system while reducing possible side effects with decreasing in frequency of dosing is included in this category and most probably achieved by using suitable polymers and generally restricted its usage for oral route of administration. Further this type of dosage form doesn’t target particular body sites or parts of a system, often they can either be released immediately or in small

amounts after administration and even extend the drugs half-life. Suffix SR is used and to some extent is generic term. Further, to treat chronic disease conditions prolonged periods of drug usage, often for the rest of their life this type of dosage form used as extended release.

3. Controlled release system: Controls the rate of drug release within a specific period of time by predetermined pattern of drug release and usually follows zero order kinetics. Concentration of drugs in plasma constantly maintained and not depended on the biological environment of the application site. This means in controlled release dosage form they are not just controlling release rate of a dosage form, controlling the drug concentration in the body. Further compared to generic term sustained release (SR) dosage forms restricted oral usage, it can be used in various routes of administration including transdermal, vaginal and oral routes. Suffix CR is used

4. **Prolonged release system:** It is developed to deliver a continuous supply of drug over a long period of time by slow release of the medication from the drug products by preventing rapid absorption of the drug which results in extremely high peak plasma concentration. Further, in this dosage form peak and trough drug levels exist in the body due to the rate of drug elimination could not match with drug release from the product.Prolonged action tablets similar to first-order release products and typically differ from that, peak is delayed differently.

5. Targeted Release system (smart drug delivery system):The direct delivery of a medication to a particular biological site or near the site of action, it may bethe capillary bed of predetermined targeted site such as complete organ or tissue or cavities (first order targeting) or specific cell such as tumor cells not to the normal cell,receptor (second order targeting)or at cellular, subcellular level interaction of the target cell (third order targeting) with control over the distribution of a drug with in the body.The developed dosage form may have either immediate or modified release characteristics. Targeting of drugs achieved by using existing natural distribution mechanisms with in the body caused by physicochemical or pharmacological signal called as passive targeting or targeting groups such as antibodies and ligands to direct the system to the particular site called as active targeting and the use of monoclonal antibody for cancer treatment is an example for this type of drug delivery system.[5,6]

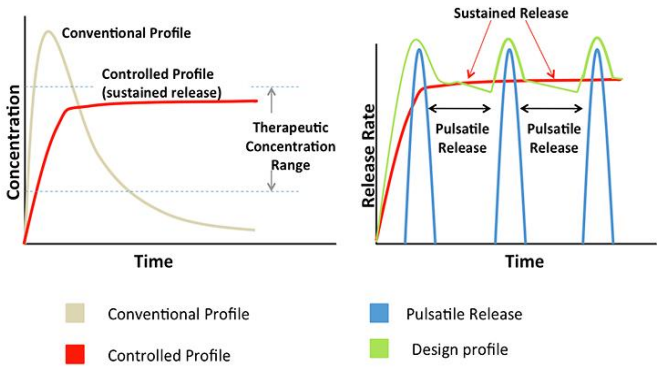
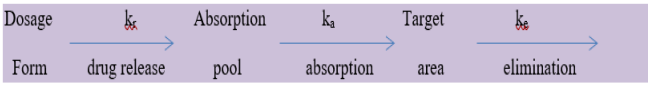


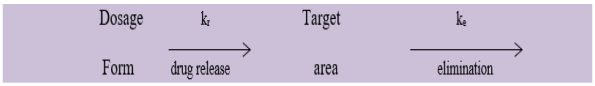
Figure.1: Plasma drug concentration-profile shows the relationship between controlled release,prolonged release, conventional- release drug delivery.

II. SUSTAINED RELEASE DRUG THERAPY:[7]

As was already mentioned, conventional dosage formulations are thought to quickly release their active components into an absorption pool. The following straightforward kinetic scheme illustrates this.



The absorption pool represents a drug solution at the absorption site, Kr, Ka, and Ke implies the first-order rate constants for drug release, absorption, and overall elimination, respectively. The drug is released immediately form dosage shows that Kr >>> Ka. Drug release from the dosage form, is the rate-limiting step for non-immediate release dosage forms i.e.,kr<<<ka. As a result, the kinetic scheme described above is reduced to[8]



The rate of delivery must be constant over time and independent of the amount of drug remaining in the dosage form. Which means the drug released from the medication must follow zero-order kinetics,as mentioned in the equation:[9]

K_r^0 = Rate In = Rate Out = $k_e.c_d.v_d$

- K_r^0 →Zero order rate constant for drug release
- k_e→ First order rate constant for overall drug elimination
- c_d → Desire drug level in the body

- v_d→ Volume space in which the drug is distributed

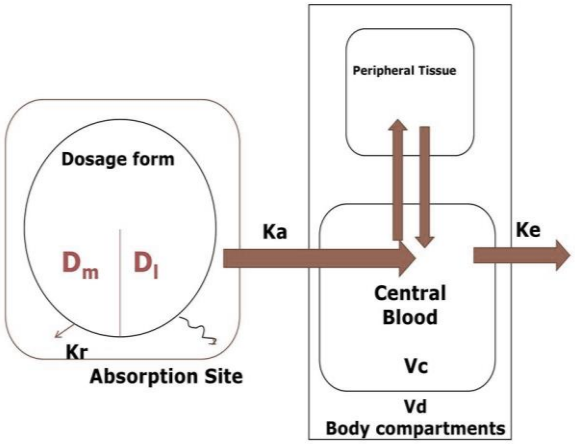


Figure.2: A general pharmacokinetic model of per-oral sustained release dosage form. [10]

III. FACTORS AFFECTING SUSTAIN RELEASE DOSAGE FORM:

A. Biological factor:

1) Biological half-life:

The usual goal of an oral sustained-release product is to keep therapeutic blood levels stable over time. The half-life quantitatively describes the elimination rate.A drug with a biological half-life of 2-8 hours is considered as good for the candidates because it can reduce dosing frequency. However, drugs with extremely shorter biological half- lives may require large amounts of drug in each dosage unit to maintain sustained effects, forcing the dosage form itself to become prohibitively large. The drug should maintain a half-life of 3-4hours.[11]

2) Absorption:

A drug's absorption characteristics can have a significant impact on its suitability as a sustained-release product. Because the goal of developing a sustained-release product is to exert control over the delivery system, the rate of release must be much slower than the rate of absorption. If we assume that most drugs and devices have a transit time of 8-12 hours in the absorptive areas of the GI tract, the maximum half-life for absorption should be around 3-4 hours; otherwise, the device will pass out of the potential absorptive regions before drug release is complete. This corresponds to an apparent absorption rate constant of 0.17-0.23 hours-1 over this time period, yielding 80-95%. The apparent rate constant is the absorption rate constant.[12]

3) Distribution

A drug distribution into tissues can play an major role in the overall kinetics of drug elimination. Because it not only lowers circulating drug concentrations but can also be rate limiting in its equilibrium with blood and extravascular tissue, apparent volume of distribution varies with the time course of drug disposition. As a result, knowledge of drug disposition is required for the development of sustained release products.[11]

4) Metabolism:

Drugs that are significantly metabolized prior to absorption, whether in the lumen or tissue of the intestine, may have lower bioavailability than slower-releasing dosage forms. Most enzyme systems in the intestinal wall are highly potent. Because the drug is delivered to these regions at a slower rate, less total drug is exposed to the enzymatic process during a given time period, allowing for a more complete conversion of the drug to its metabolites. Another viable option is to formulate these enzymatically susceptible compounds as pro-drugs.[13]

B. Physiochemical factors:

1) Dose size:

For a conventional dosage form, a single dose of 0.5 - 1.0 g is considered as a range limit. The same limit is maintained for sustained release dosage forms. Another factor to consider is the margin of safety involved in administration of large quantity of drug with narrow therapeutic range.[14]

2) Aqueous solubility and pka: Aqueous solubility:

The reported lower limit for a drug's solubility in a sustained release system is 0.1 mg/ml. The administered drug should get dissolve in the aqueous medium first and then partition into the absorbing membrane.it is explained by Noyes Whitney's equation.[15]

$Dc/dt = K_dAC_s$

Where, dc/dt ─ Dissolution rate
K_d─ Dissolution rate constant
A ─ Total surface area of drug
C_s─Aqueous saturation solubility.

Pka: Pka of the compound and Ph of the medium govern the aqueous solubility of the weakly acid and weakly basic drugs.

In stomach absorption, weakly acidic drugs are in unionized form and favors acid medium. For weakly basic drugs it exists in ionized form and favors alkaline medium.[16]

3) Partition coefficient:

When a drug is administered to the GI tract, it must cross a number of biological membranes in order to have a therapeutic effect elsewhere in the body. Because these membranes are commonly made up of lipids, the partition coefficient of oil soluble drugs becomes important in determining the effectiveness of membrane barrier penetration. The reported lower limit for a drug's solubility in a sustained release system is 0.1 mg/ml.Therefore, oil by water partition coefficient plays a major role in evaluating the penetration of drug. [17]

K =Co/Cs

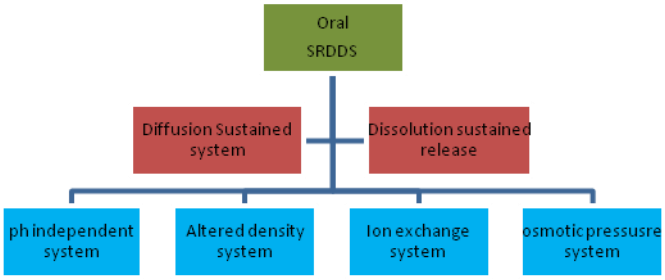
Where, Co =Equilibrium concentration in organic phase.

Cs =Equilibrium concentration in aqueous phase

4) Drug stability:

Degradation of solid dosage form is much slower compared to liquid and suspension. Drugs that are taken orally can be subjected to acid-base hydrolysis as well as enzymatic degradation. Systems that extend delivery over the entire course of transit in the GI tract are beneficial for drugs that are unstable in the stomach. To avoid such degradation drugs are incorporated in polymeric matrix.[18]

IV. STRATERGIES FOR THE DEVELOPMENT OF SUSTAINED RELAESE DOSAGE FORM: [19,20,21,22]



1.Diffusion sustained release:

Diffusion of dissolved drug via a polymeric membrane is a rate-limiting phase in diffusion release models. Due to the fact that the diffusional path length elongates with duration as the insoluble matrix becomes drug deficient in this system, the drug release rate never exhibits zero-order kinetics. The transfer of drug molecules from an area of higher concentration to a region of lower concentration is represented by the diffusion process' mechanism.

$dm = ADK\Delta C / dt L$

Where,A = Area.

K = Partition coefficient of drug between the membrane and drug core.

L = Diffusion path length (i.e., thickness of coat).

ΔC = Concentration difference across the membrane.

a) Reservoir diffusion control:

A drug core is enclosed in this system by a water-insoluble polymeric substance. Upon entering the polymer membrane, the drug will exchange with the fluid surrounding the particle or tablet**.**

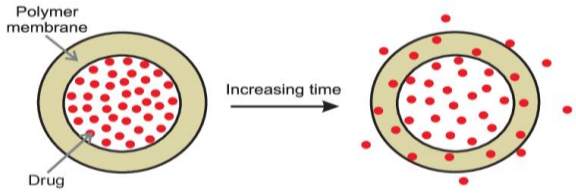


Figure.3: Schematic representation of diffusion sustained drug release- reservoir diffusion control

b) Matrix diffusion control:

These systems are hollow, with a drug-filled inner core encased in a membrane made of a water-insoluble polymer. Either by travelling through pores or between polymer chains, the medication is released.

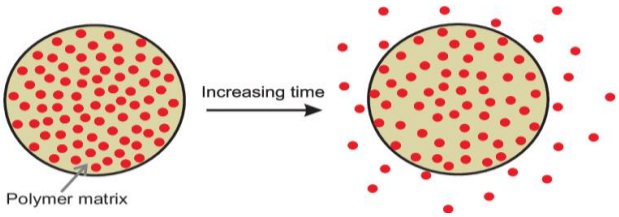


Figure.4: Schematic representation of diffusion drug release-matrix control

2. Dissolution controlled:

These systems are simple to construct. Drugs that are created utilising a system produce slow-dissolving forms with gastric and intestinal fluids as well as medications with a high rate of water solubility and dissolution

J = -D dc /dx

Where, J = flux of the drug across a membrane in the direction of decreasing conc.
D = Diffusion coefficient of the drug.
dc /dx = Change in the concentration of the drug in the membrane

There are two distinct categories of dissolution-controlled release systems:

A. Matrix/Monolith Dissolution System.
B. Encapsulation/Coating/Reservoir System.

A. Matrix dissolution system:

Due to the homogeneous distribution of the drug in a rate-regulating medium, these devices are also referred to as monoliths. Bee wax, carnauba wax, and other types of wax are used to regulate the degree of dissolution.

The fundamental mechanisms govern the rate of dissolution:

• Modifying the tablet's porosity to change the rate at which fluid penetrates the tablet.
• Reducing the tablet's ability to get moistened.
• Polymer breakdown is slowly occurring.

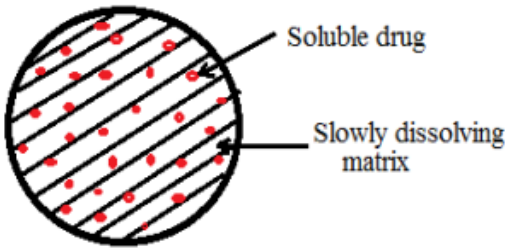


Figure 5: Diagrammatic representation of soluble matrix system

B. Reservoir dissolution system:

In reservoir systems, the active material are coated or encapsulated using one of the microencapsulation processes with slowly dissolving materials like cellulose, polyethylene glycol, and waxes. This substance may be compacted into tablets or encapsulated in capsules. A significant factor in the rate of medication dissolution is its solubility and coating thickness.

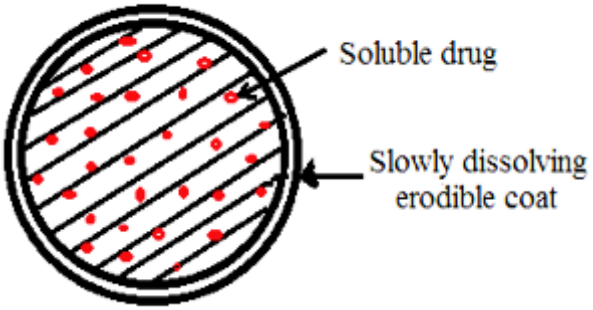


Figure 6: Diagrammatic representation of soluble reservoir system

3. Ph dependent system:

These systems are made to deliver medications to the intestinal tract that are acid-labile or that irritate the GIT mucosa. It is created by covering the tablet's core with a mixture of intestinal fluid soluble and insoluble polymers (ethyl cellulose) (HPMCP). The coated barrier prevents the medicine from dissolving in the stomach when the pH is acidic. The system moves to the small intestine after stomach emptying. The intestine-soluble component dissolves at pH levels higher than 5, creating a porous membrane that regulates the release of the medicine from the tablet's core.

4. Altered density system:

The average transit time for gastrointestinal contents is under 24 hours. This is a significant design constraint for prolonged release formulations. The frequency of dose can be further decreased if the drug's duration in the stomach or intestines is extended. This could be accomplished by changing the size of the dosage form, the density of the drug particles, or the use of mucoadhesive polymers.

This system is further classified into:

A. high density approach:

Since GI fluids have a density of roughly 1.4 g/cc, drugs with particle densities greater than this value—typically 1.6 g/cc—can be utilised for this purpose. These systems can stay in place for a long period and are unaffected by eating. For this, iron oxide and barium sulphate might be employed.

B. Low density approach:

Compared to GI fluids, these pellets have a lesser density. As a result, the drug release is slowed down since such tablets have a tendency to float on stomach juice for a long time. A medication can be granulated with 20–80% hydrogel, such as HPMC, HPC, and HEC, to create such a system. Tablets swell and create a diffusible gel barrier when they come into touch with GI fluids, which causes the system's density to drop below 1 and enable floating.

5. Osmotic Pump System:

These systems, which follow the osmotic pressure mechanism and release the medicine at a constant zero order rate, are also referred to as oros. The medicine is combined with an osmotic agent, such as mannitol or KCl, in a reservoir that is encircled by a semipermeable membrane. The dosage form has a small opening that allows water to enter the reservoir and aids in the dissolved medicine being pumped out at the predetermined rate due to osmotic pressure. The GIT's internal conditions have little impact on how quickly the medicine releases from the reservoir. The size of the aperture, the thickness of the semipermeable membrane, the permeability of the membrane, the osmotic characteristics of the core, and the stability of the drug all affect how much medication is released.

6. Ion Exchange System:

This kind of technology has evolved for regulating the speed of distribution of ionisable or ionic medications and is based on the idea that the GIT has a generally constant number of ions. The drug resin solution can be incubated or run through a column containing exchange resin to create such a system. A resin containing a SO3- group is used to complex cationic drugs, and a N(CH3)3 group-carrying resin is utilised to complex anionic drugs. The sustained release tablet's hydronium and chloride ions diffuse into the GIT and interact with the medicine's resin compound to cause the release of the drug.

Types of ion exchange resins:

Cationic exchange resin: Contains acidic functional group.
Anion exchange resin: Contains basic functional group.

When a drug is exposed to resin for a long time, a drug-resin complex is created. The medication included in these complexes is altered in the digestive system before being released along with an excess of Na+ and Cl-.

$Resin^{-} – Drug^{-} + Cl^{-} \rightarrow resin^{+}\ Cl^{-} + Drug^{-}$
Where xis Cl^{-} conversely

$Resin^{-} – Drug^{+} + Na^{+} \rightarrow resin^{-}\ Na^{+} + Drug$

For this system, cross-linked polymer molecules that are insoluble in water are utilised.

V. MATRIX TABLET

Matrix system implies that "A homogenous dispersion of the drug particles in either a lipophilic or a hydrophilic polymer matrix creates the drug reservoir in this sort of controlled drug delivery system". This system is widely employed in constructing sustained release dosage form, which works by releasing the dosage in two mechanisms either by diffusion or dissolution.[23]

VI. SUSTAINED RELEASE MATRIX TABLET

One of the simplest techniques for producing sustained release dosage forms are direct compression of the medication, the release retardant, and the additives to create a tablet. The drug embedded in a matrix core of the release retardant is one of the simplest techniques for producing sustained release dosage forms. As an alternative, the drug retardant mixture could be granulated before compression.[24]

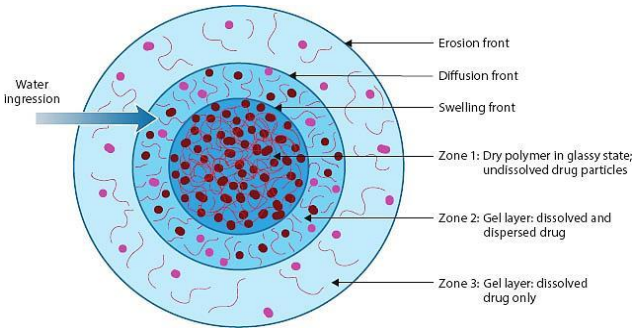


Figure7: Schematic representation of Sustained release matrix system

The creation of matrix tablets involves the employment of three different classes of release retarding substances.

1. Insoluble or 'skeleton' matrices
2. Water insoluble, erodible matrices
3. Hydrophilic matrices.

A. <u>Merits:</u> [25,27]

- Simple to produce
- versatile, efficient, and inexpensive
- Made to release molecules with a high molecular weight.

- The therapeutic concentrations may be sustained for extended periods of time with the sustained release formulations.
- Utilizing formulations with a sustained release helps reduce high blood concentration.
- Formulations with sustained release may increase patient compliance.
- Drug absorption can be slowed to lessen toxicity.
- By preventing the medicine from being hydrolysed or undergoing other derivative modifications in the digestive tract, you can increase stability.
- Reduce the negative local and systemic consequences.
- A rise in the effectiveness of treatment.
- Drug build-up can be reduced with persistent dosage.
- Increasing some medicines' bioavailability.

B. Demerits: [26,27]

- After the medicine has been released, the residual matrix needs to be removed.
- High preparatory costs.
- Food and the velocity at which it travels through the gut are two elements that have an impact on release rates.
- The square root of time affects how quickly drugs are released. Due to a rise in diffusional resistance and/or a fall in effective area at the diffusion front, release rate continuously decreases. However, using extremely slow-release rates which in many cases are identical to zero-order—can result in a significant persistent effect.

VII. MANUFACTURING TECHNIQUES OF MATRIX TABLET: [27,28]

1) Direct compression:

Direct compression (DC) is the simplest manufacturing process with the fewest processes, making it the least expensive and easiest to control. The API and excipients are blended, and the completed tablets are compressed, in the two main processes of the direct compression tablet process.

2) Dry granulation:

Roller compaction and slugging are the two forms involved in this process. In the slugging procedure, the granule is squeezed again and the slugs are broken down to create granules. The powder is recompressed with pressure rolls during roller compaction, in contrast.

3) Wet granulation:

This approach involves mixing a sufficient amount of granulating agent with the measured quantity of the medicine and excipients. The moist weight is taken into consideration once there has been sufficient solidification. Using a single punch tablet compressor, the dried granules are combined with lubricant and disintegrant to create compressed "flowing powder" tablets after being checked for dry granules.

4) Steam granulation:

Instead of using water, steam serves as the granulation's binder. It diffuses and spreads evenly throughout the granules. More surface area makes the granules rounder, which increases the pace at which drugs dissolve from granules**.**

5) Melt granulation:

The material, which melts at low temperatures, is used in this technique. By dissolving it over the substrate and then heating it above its melting point, this chemical can be added. Granular solutions were used to test various lipophilic bonds.

6) Hot-Melt Extrusion Process:

A mixture of active substances, thermoplastic polymers, and other processing materials are poured into the extruder barrel during the hot-melt extrusion process using a hopper. A rotating screw moves the materials inside the heated pipe. With an asset attached to the end of the barrel, soluble compounds at high temperatures and the molten mass are continually treated. The extrude method can also be used to manufacture films, depending on the size of the die cylinders.

7) Freeze granulation:

Spraying slurry into liquid nitrogen causes droplets to instantly freeze into granules, which is followed by the drying process known as lyophilisation.

VIII. POLYMERS USED IN MATRIX TABLETS

- **Hydrogelspolymers:** Polyhydroxyethyle methyl acrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Cross-linked polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA).

- **Solublepolymers:** Polyethyleneglycol (PEG), polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC).
- **Biodegradable polymers**: Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), Polyanhydrides, Polyorthoesters.
- **Non-biodegradablepolymers**: Polyethylene vinyl acetate (PVA), Polydimethylsiloxane(PDS), Polyether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC)
- **Mucoadhesivepolymers:** Polycarbophil, Sodium carboxymethyl cellulose, Polyacrylicacid, Tragacanth, Methyl cellulose, Pectin
- **Natural gums:** Xanthan gum, Guar gum, Karaya gum, Locust bean gum.

IX. CLASSIFICATION OF MATRIX TABLETS:

[29,30,31]

1.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.

2.On the basis of porosity of matrix

a) Macro porous system
b) Micro porous system
c) Non porous system

1. A) Hydrophobic matrix system: The primary factor in nature that controls rate is the hydrophobic matrix, which is insoluble in water. Included in these elements are waxes,glycerides, fatty acids, and polymeric substances such acrylate copolymers, ethyl cellulose, and methyl cellulose. The hydrophobic matrix system's ability to deliver at a controlled rate has grown in significance. For drugs with restricted therapeutic indices, constant rate drug delivery has long been one of the main goals of controlled release systems.

B) Hydrophilic matrix system:

The hydrophilic matrix polymer's main rate-limiting components swell upon contact with an aqueous solution and produce a gel layer on the system's surface. The solvent permeates into the empty space between macromolecular chains when the releasing medium (in this case, water) is thermodynamically compatible with a polymer. Due to the stress of the solvent penetrating during the relaxation phase, the matrix expands and the polymer chain becomes more flexible. Important polymers like xanthan gum, Carbopol 940, and alginates have been employed in hydrophilic matrices, along with HPMC (Hydroxy propyl methyl cellulose) and HPC (Hydroxy propyl cellulose). When directly compressed, HPMC and HPC polymers can exhibit good compression characteristics due to their special features. They have a high amount of drug loading and are non-toxic.They have swelling capabilities that make it possible to quickly produce an exterior gel layer, which is crucial for the regulated release of drugs.

C) Fat-wax matrix system:

Spray congealing in the air, bleeding congealing in the aqueous medium with or without the help of the surfactant, and the spray drying method were used to include the medicine into the fat wax granulation process. By compacting with a roller compactor, heating in an appropriate mixture such a fluidized bed and steam jacket blender with a solution of a wax material, or by using another blender, the mixture of active medicinal ingredients, wax materials, and filter can be transformed into granules. The amount of the total drug that can be incorporated into a matrix and the drug release can both be affected by the addition of surfactant to the formulation.

D) Biodegradable matrix system:

These polymerization matrices, which are made up of monomers, have been joined together by functional groups and weak linkages in the backbone. They have been destroyed by enzyme and created by surrounding cell or organ, non-enzymatic process into oligomers and monomers in the biological system. Examples include synthetic polymers such as aliphatic polyesters, polyanhydrides, polycaprolactone, and natural polymers such as protein, polysaccharides, modified natural polymers, and so on.

E) Mineral matrices:

Mineral matrices are made up of polymers that come from different kinds of seaweed. Example: Using diluted alkali, several species of brown seaweeds (Phaephyceae) can produce alginic acid, a hydrophilic carbohydrate.

2. A) Macro porous system:

The medication diffuses in this system through matrix pores with a size range of 0.1 to 1mm. This size exceeds the size of the diffusion molecule.

b) Micro porous system:

They have occurred through pores in this type of system. A microporous structure with pores that ranges from 50 to 200 A^0 is slightly bigger than the size of diffusing molecules.

c) Non porous system:

In this system, there are no pore phases. Only one polymeric phase occurs and the molecules diffuse through the network meshes

X. MECHASIM OF ACTION MATRIX TABETS

The diffusion or disintegration of the medication is one of the mechanisms involved in its release. Hydration of the matrix occurs when it is exposed to an aqueous solution; as a result, it swells to close off any existing pores and the contents dissolve. Gel formation results in the production of a viscous solution, which creates a positive pressure that prevents liquid entrance and leads to matrix disintegration**.** The matrix swells, causing drug release via diffusion from the matrix and matrix erosion, as demonstrated in figure: 8

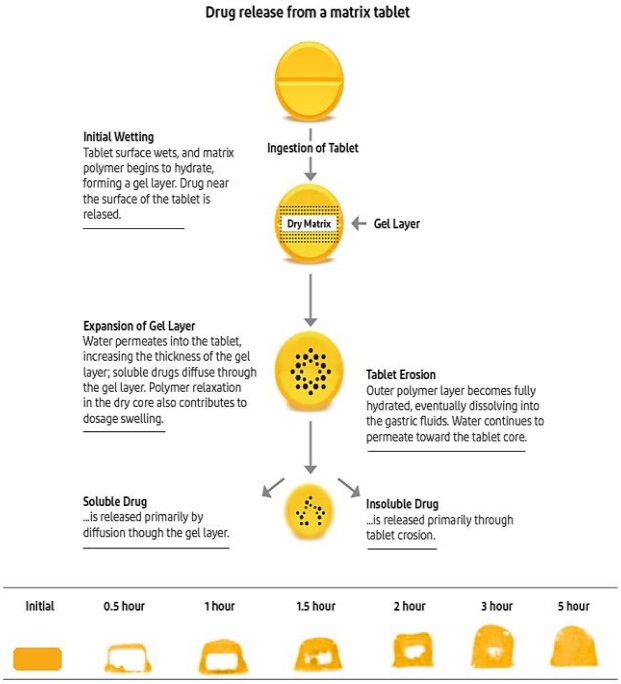


Figure8: Mechanism of drug release from hydrophilic matrix tablet

Evaluation of Sustained release Matrix tablets:[33]

Before a sustained release product is marketed, its strength, safety, stability, and dependability must be established by in vitro and in vivo testing.

I)Per-compression studies:

1) Angle of repose: Flow property was determined by measuring the angle of repose. The funnel method was used to calculate the angle of repose of granules. Granules were allowed to freely flow through the funnel and onto the surface and the powder cone's diameter was measured.

$\tan(\Theta) = h/r$

Where, Θ = Angle of response

h = Height of heap

r = radius of pile

2) Bulk density: Bulk density is a ratio of given mass of powder and its bulk volume.

$\text{Bulk density} = M/V_0$

Where, M =Mass of the powder

V_0= Bulk volume of powder

3) Tapped density: It is generally given by the equation.

$\text{Tapped density} = M/V_r$

Where, M = mass of the powder

V_r= Final tapping volume of powder

4) Compressibility index and Hausner ratio:

To determine the powder's unsettled apparent volume (V0) and final tapped volume (VF) after tapping the substance until no more volume changes occur. This is provided by the following expression.

$$\text{Compressibility index} = \frac{\text{1- Bulk density}}{\text{Tapped density}} \times 100$$

$$\text{Hausner's ratio} = \frac{\text{tapped density}}{\text{Bulk density}}$$

II)Post- compression studies:

Weight variation: Twenty tablets were weighed individually and then grouped together to determine their average weight.

Hardness: Monsanto's hardness tester was used to measure the hardness of tablets from each batch, and average values were computed.

Friability: The Roche friabilator, which rotates at 25 rpm for 4 minutes, was used to assess the tablets' potential to become friable**.**

Thickness: Using a micrometre screw gauge, the thicknesses of the tablets were measured.

Content uniformity: The quantity of the medication was discovered using a UV-visible spectrophotometer and the calibration curve approach.

Kinetic Studies:

In-vitro dissolution studies: Rotating Paddles equipment is typically used to determine drug release studies. Buffer is primarily utilised as a dissolving media. The dissolution medium in which the medication is released is sampled as needed at regular intervals, and the same quantity of the medium is replaced, all while maintaining the bath's temperature at 370C. An UV spectrophotometer is used to measure the quantity of the medication emitted. The % release of a drug at a certain moment is plotted against time**.**

Stability studies: Short Term Stability Investigation: The best batch underwent a short-term stability study to ascertain how the in vitro release profile changed upon storage.

In-vivo methods: It becomes vital to conduct in-vivo evaluation and establish in-vitro in-vivo correlation once the desired in-vitro profile has been obtained. The different in-vivo evaluation techniques include

- Clinical response
- Blood level data
- Urinary excretion studies
- Nutritional studies
- Toxicity studies
- Radioactive tracer techniques

XI. CONCLUSION

There are various reasons for appealing this sustained release matrix tablets. It increases drug product bioavailability, reduces frequency of administration to extend the duration of effective blood levels, reduces peak through concentration fluctuation and side effects, and possibly improves drug specific distribution. This involves in reducing the dose for long term users with infections, diabetes, hypertension etc., and delivering the drug to the targeted and minimizing the side effects.

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