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Review Article

A Review on Sustained Drug Delivery System: Matrix Tablet

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Abstract

A wide range of tangible and intangible advantages have been accrued to patients as a result of the widespread use of pharmaceuticals with sustained release. Another possible way to lessen the medication's side effects is with continuous release, which limits changes in the therapeutic concentration of the drug in the body.. These days, very few drugs emerge from research and development, and those that do have resistance issues stemming from their overuse—particularly antibiotics, which are used erratically—are the result. Therefore, by slightly altering the drug delivery, a change in operation is a suitable and optimal way to increase the effectiveness of some drugs. Another effective method for reducing side effects is sustained release.

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Introduction

The most common method of drug administration is oral, which is partly because it is the easiest to use and partly because gastrointestinal physiology allows for more design flexibility when creating dosage forms than most other methods. Drug delivery systems that slow the release of medicine over an extended period of time following a single dose are known by a variety of names, but their primary goal is to achieve or prolong therapeutic impact. Common terms for these formulations include depot, sustained, prolonged, modified, and extended release. The pharmaceutical industry has known for a long time that a single dose that is released gradually over time is preferable than providing many doses of a medicine. [1]

The major Drawback Associated with Conventional Dosage Forms[2]

- Lack of adherence among patients increases the likelihood that they will miss a dose of a medicine with a short half-life, necessitating repeated administration.
- Undermedication or overmedication might occur as a result of the inevitable changes in drug concentration.
- It is challenging to achieve steady-state conditions because a typical peak-valley plasma concentration time profile is obtained.

A new breakthrough for innovative drug delivery methods has been made in the pharmaceutical technology industry thanks to the matrix tablet's sustained release (SR) (NDDS). The amount and kind of polymer utilised in the formulations mainly regulate the medication release rate from the dosage form; complicated production procedures such as coating and palletization are not incorporated. It is common practice to use hydrophilic polymer matrix for developing SR dosage forms. The commercialization of new pharmacological entities is costly and complicated, hence there has been a shift in focus toward developing drug delivery systems with controlled or sustained release. One typical application of matrix systems is sustained release. The release mechanism controls and prolongs the release of the drug. [3]

Matrix Tablets

The active and inactive ingredients are mixed and dispersed evenly throughout the dosage form in a matrix method. For many reasons, matrix systems have become the gold standard in oral extended-release technology. The release from matrix type formulations is governed by Fick's first law of diffusion. Particles of the medicine are dispersed throughout a porous matrix composed of either hydrophilic (wax, sodium carboxy methylcellulose, hydroxy propyl cellulose, methylcellulose, and wax) or hydrophobic (polyethylene, polypropylene, ethyl cellulose, and polyethylene) polymers. The drug and other substances, such as solvents, are arranged in a three-dimensional structure called a "matrix" in this context. [4]

SustainedReleaseDrugDeliverySystem

"Sustained release" is a commonly used term to describe a type of pharmaceutical dosage form that gradually releases a therapeutic agent. This helps to maintain the loading dose, solubility of the polymer, diffusivity within the polymer matrix, and porosity of the release unit plasma profile over time. [5]

Limitations of Matrix System

Matrix systems are limited, just like any other technology. Initially, matrix systems are not adaptable enough to change dosage levels on a regular basis as needed to meet clinical study objectives. More often than not, a new formulation and consequently more resources are anticipated when a new dosage strength is determined to be required. Furthermore, more sophisticated matrix-based technologies Certain products require stacked tablets due to their particular release profiles (dual release or delayed plus extended release). The purpose of a matrix formulation is to achieve release of an active ingredient, such as a pharmaceutical, by continuously leaching it from an inert matrix core. The active ingredient is typically incorporated in insoluble excipients. [6]

Matrixsystemscanbedividedintothreetypes:

1. Monolithicmatrixtablets
2. Gelforminghydrophilicmatrixtablet
3. Erodible(hydrophobic) matrix tablets

Inertmonolithic matrixtablets:

Including a medication in an inert matrix is arguably the easiest way to achieve a continuous release of a medication from an oral dose form. When something is inert, it doesn't interact with the biological fluids. Due to the fact that the drug release from plastic matrix tablets is not dependent on the digestive juices' state or condition—which can vary greatly between and within patients in terms of pH and viscosity—this leads to its widespread use. The skeletal structure of the porous matrix tablet can be found in the feces because it does not break down like regular tablets do when passing through the gastrointestinal tract. Primarily, lipophilic compounds and (insoluble) polymers are utilized in the creation of these inert matrices. Initial polymers utilized in the process of preparing. [7]

Gel-forming hydrophilic matrix tablets:

Medications are distributed in a swellable hydrophilic polymer in systems that generate homogeneous or heterogeneous gels. Because these systems permit long-term, continuous medication delivery, they have been the subject of substantial research. Drug release is influenced by polymer properties.. Ingesting gel-forming hydrophilic matrix tablets causes the hydrophilic polymer to undergo plasticization in the aqueous gastrointestinal tract, leading to volume expansion and relaxing of macromolecular chains. Consequently, when the gastrointestinal fluids have permeated the tablet, a transparent front separating a wet, rubbery gel layer from a dry, glassy core becomes visible. The swelling of the gel regulates the release of the dissolved medication. [8]

Erodible matrix tablets:

Polyanhydrides and other erodible polymers present an additional intriguing material platform for zero order drug release. Similar to a few HPMC grades, polyanhydrides create a gel layer that erodes at a particular rate when water penetrates it. The gel layer's thickness can be kept constant over time by selecting the appropriate polymer composition. [9]

Sustained Release Oral Dosage Forms:

Not every medication can be made into a sustained release product, and not every medical condition can be treated with one of these products. When deciding whether to create a sustained release dosage form, the medication and the therapeutic indication must be taken into account simultaneously. [10]

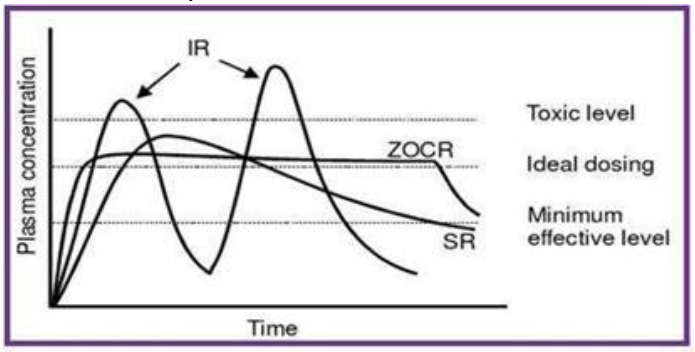

Fig 1: Characteristic representation of plasmaconcentrations of drug

Modern pharmaceutical design now adheres to controlled release drug delivery standards, and extensive research has been done to improve the effectiveness, safety, and dependability of drug products. The majority of drug delivery systems will still be composed of oral sustain release medication. Thus, the goal of this work is to formulate tablets with a higher bioavailability while avoiding first pass metabolism. Therefore, a sustained release system formulation attempt was made in this work to achieve an even plasma concentration profile for up to 24 hours. [11]

- It is very permeable and has a poor solubility in water, making it a BCS class II medication. And maintaining the drug's release is essential.
- Oral ingestion results in a 20% bioavailability. Formulation in sustain-release tablets involves discrete features.
- Lessriskofdosedumping.

Advantages of Matrix Tablet [12]

- Easy to manufacture
- Versatile, effective and lowcost
- Can be made to release high molecular weight compounds
- The sustained release formulations may maintain the rapeutic concentrations over prolonged periods.

- The use of sustain release formulations avoids the highblood concentration.
- Sustain release formulations have the potential to improve the patient compliance.
- Reduce the toxicity by slowing drug absorption.
- Steer the medicine away from hydrolysis and other derivative changes in the gastrointestinal tract to make it more stable.
- Minimize the local and systemic side effects.
- Improvement in treatment efficacy.
- Minimized rugaccumulation with chronic do sing.
- Usage of less total drug.
- Improvement the bioavail ability of some drugs.
- Improvement of the ability to provide special effects.

Terminology:

long-term and manageable A lot of people have been using the words release and release in a way that doesn't make sense. They each represent a distinct mode of delivery. A drug delivery system that either shows the system can give some therapeutic control (spatial or temporal) or a dose form that delivers medication over a long period of time. [13]

Modified Release Drug Product:

The phrase "updated release" The term "drug product" refers to goods that modify the drug substance's release schedule or rate. [14]

Extended-Release Dosage Forms:

The ability to reduce the frequency of dosing by at least two times when compared to the drug delivered in an immediate-release (traditional) dose form. Long-acting pharmaceutical medicines, controlled-release pharmaceuticals, and sustained-release pharmaceuticals are all examples of extended-release dose formulations. [15]

Sustained release:

It comprises all drug delivery methods that accomplish gradual drug release over a long period of time, not just at a set pace. [15]

Controlled Release:

It includes all methods of medication administration where the medicine is given at a set rate over a long period of time. [14,15]

Delayed Release Dosage Form:

Even though some medications release their full potency right after injection, dosage forms release their individual doses at predetermined intervals rather than all at once. Dosage forms that are coated with enteric are one example. [14]

Repeat Action Dosage Forms:

The drug is released in two doses: one at the beginning of the treatment and another at a later time. It is a form of modified release medication product.. [16]

Prolonged Action Dosage Forms:

This medication delivery system is engineered to release the drug gradually, ensuring a steady supply for a long duration.[15]

Classificationof MatrixTablets:

On the Basis of Retardant Material Used:

1. Hydrophobic Matrices (Plastic matrices):

The idea of using inert or hydrophobic materials as matrix components was initially put forth in 1959. For oral dosage forms that enable prolonged release, this method compresses a drug mixture with a hydrophobic polymer into a tablet. The medicine has been released gradually over time after diffusing through a system of channels within the compressed polymer particles. Polyethylene, ethyl cellulose, polyvinyl chloride, acrylate polymers and their copolymers, and other similar compounds have been used as hydrophobic or inert matrices. In these formulations, the rate is controlled by the liquid penetrating the matrix. One possible way that these tablets release their drugs is through diffusion. These specific kinds of matrix tablets eventually become dormant.[17]

2. Lipid Matrices:

Using lipid waxes and related compounds, these matrices were constructed. The medication can be released through erosion or pore diffusion in these matrices. Hence, the release properties are more

affected by the digestive fluid's composition than by the totally insoluble polymer matrix. Combinations of carnauba wax and stearyl alcohol or stearic acid have been utilised as retardant bases in numerous sustained release formulations. [18]

3. HydrophilicMatrices:

Due to their adaptability in achieving a desired drug release profile, affordability, and regulatory acceptance, oral controlled drug delivery systems based on hydrophilic polymer matrices are extensively utilised. Particularly relevant in the controlled release field is medication formulation in gelatinous capsules or, more commonly, tablets using hydrophilic polymers with significant gelling characteristics as base excipients. A gelling agent, often known as a hydrophilic polymer, and a drug or drugs are well-combined in an infected matrix. Swellable. [19]

controlled release systems are the name given to these systems. Cellulose derivatives:

- Methylcellulose 400 and 4000 cPs
- Hydroxy ethyl cellulose
- Hydroxy propylmethylcellulose (HPMC) 25, 100, 4000, and 15000 cPs
- Sodium carboxymethylcellulose [20

Polymers of acrylicacid:

Polymers which areuse dinacrylic acid category is Carbopol 934.

Other hydrophilic materials used for preparation ofmatrix tablet are Alginic acid, Gelatin and NaturalgumsFat-waxmatrixtablet: [20]

Fat wax granulations can have the medicine added to them by spray-drying, blend-congealing in a watery medium with or without a surfactant, or spray-congealing in the air. When the medication suspension and melted fat-wax are combined during bulk congealing,. After the combination has solidified, it is crushed into sustained-release granulations. Alternatively, the mixture of fillers, waxy materials, and active substances can be heated in the right combination (such a fluidized-bed and steam jacketed blender), compacted with a roller compactor, or ground into granules using a waxy material or another binding solution. Leaching, hydrolysis, and/or enzyme-induced fat dissolution release the medicine from a wax-and-fat melt. [21]

BiodegradableMatrices:

Polymers having monomers linked together via functional groups form these, which have unstable backbone connections. Enzymes produced by the surrounding living cells break them down or erode them biologically to make them more amenable to metabolism or elimination, a non-enzymatic process breaks them down into smaller pieces called oligomers and monomers. Proteins and polysaccharides are modified natural polymers, while aliphatic poly (esters) and poly anhydrides are examples of manmade polymers. [22]

Mineral Matrices:

Polymers derived from several types of seaweed make up these. Use of weak alkali to extract a hydrophilic carbohydrate from brown seaweed (Phaeophycean) species is one example. One such carbohydrate is alginic acid. [23]

Polymers Used In Matrix Tablet.

Hydrogels:

Polyhydroxylethylmethylacrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Crosslinkedpolyvinylpyrrolidone (PVP), Polyethyleneoxide (PEO), Polyacrylamide (PA). [20]

Soluble polymers:

Polyethylene glycol (PEG), polyvinyl alcohol (PVA), Polyvinyl pyrrolidone (PVP), Hydroxypropyl methylcellulose (HPMC). [20]

Biodegradable polymers:

Polylactic acid (PLA), Polyglycolic acid (PGA), Poly caprolactone (PCL), Polyanhydrides, Polyanthuses. [22]

Non-biodegradable polymers:

Polyethylenevinylacetate (PVA), Polydimethylsiloxane (PDS), Polyetherurethane (PEU), Polyvinylchloride (PVC), Celluloseacetate (CA), Ethylcellulose (EC). [22]

Mucoadhesive polymers:

Poly carbophilic, Sodiumcarboxymethylcellulose, Polyacrylicacid, Tragacanth, Methylcellulose, Pectin. [22]

Natural gums: Xanthan gum, Guar gum, Karayagum, Locust beangum. [22]

Mechanism of Drug Release from Matrix Tablet:

The medicine diffuses out of the matrix after dissolving in the outer layer that comes into contact with the bathing solution. This is happening while the bathing solution-solid medication interaction is still moving toward the inside. Diffusion control in this system requires that the drug particle dissolution rate inside the matrix be much quicker than the drug dissolved diffusion rate outside the matrix. [25]

Effect of Release Limiting Factor on Drug Release:

Whether a drug is delivered through a capsule, matrix, or sandwich type system, the rate at which it is released depends on a number of system factors, including the partition coefficient, diffusivity, diffusional path thickness, and others. [26]

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 regions. [26]

Drug solubility:

The release of drugs from swelling and erosion-controlled polymeric matrices is greatly affected by the drug's molecular size and its solubility in water. When pharmaceuticals have a reasonable water solubility, they dissolve in the infiltrating medium, but when their solubility is weak, they dissolve in two ways: first, the drug itself, and second, drug particles that have eroded their way out of the matrix tablet.. [27]

Polymer diffusivity:

The process of small-molecule diffusion in polymer structures is an energy-activated one; as the diffusant molecules acquire an adequate amount of activation energy for diffusion (Ed), they move through a sequence of equilibrium positions.. [28]

Drug loading dose:

The loading dose and drug solubility are two important factors that determine the kinetics of subsequent drug releases. As the initial drug loading increases, the absolute release rate increases monotonically, while the relative release rate initially declines and then increases; this creates a more complicated influence on the resultant release kinetics for medicines that are weakly water soluble. The porosity of the matrix grows in relation to the initial drug loading for medicines that are easily soluble in water. Because of this action, the total rate of drug transfer increases. While dealing with medications that have low water solubility, another phenomenon must be taken into account. In cases where the amount of medication at a given spot in the matrix exceeds. [29]

E. Surface area and volume:

The relationship between the surface area of the drug delivery device and the rate of drug release is well-known both theoretically and experimentally. It has been found that the surface area of the dosage form determines both the in vitro and in vivo rate of drug release. discovered that tiny tablets release their contents more quickly than huge cylindrical tablets. [30]

Biological Factors Influencing Release from Matrix Tablet [31]

- Biologicalhalf-life.
- Absorption.
- Metabolism
- Distribution
- Proteinbinding
- Marginofsafety

Biological half-life:

The typical objective of an oral SR medication is to sustain therapeutic blood levels for a long time.

This can only happen if the drug's rate of circulation entry is close to its rate of elimination. The half-life (t1/2) provides a quantitative description of the elimination rate. The total rate of removal from the bloodstream, including metabolic clearance, urine excretion, and all other processes, is unique to each drug and is known as its elimination rate. For the most part, SR formulation is a great option for therapeutic substances with a short half-life since it can decrease dose frequency. Drugs like furosemide and levodopa, which have half-lives less than two hours, are not ideal for SR preparation. Furthermore, sustaining forms of compounds with effects that last longer than 8 hours are typically not utilised. Some examples are digoxin and phenytoin.[32]

Absorption:

It is essential that the rate of release be substantially slower than the rate of absorption when creating an SR product in order to exert control over the delivery mechanism. The maximal half-life can be estimated by assuming that the transit duration of most medications in the absorption sections of the GI tract is roughly 8-12 hours. [32]

Metabolism:

Low bioavailability may occur with slower-releasing dose forms of drugs that undergo extensive metabolism prior to absorption in the intestinal lumen or tissue. Therefore, the following are requirements for the medicine to be included in the Sustained-Release dosage form: The half-life of the drug should be less than five hours.

The medicine ought to dissolve easily in water.

A longer therapeutic window would be ideal for this drug.

The GI tract ought to absorb the medicine.

The medicine and its intended formulation as an amatrix tablet containing a polymer are shown in the preceding table. [32]

It is possible to create an SR dosage form for any medication, even one with low water solubility. To achieve this goal, the medicine is first made into the SR dosage form after its solubility is enhanced using an appropriate method. Be cautious, though, because crystallisation occurs when the medication reaches the systemic circulation and must be avoided at all costs during this procedure. [34]

Distribution:

Oral SR drug delivery systems are not ideal for drugs like chloroquine that have a large apparent volume of distribution since this affects the medication's clearance rate.

Protein Binding:

The concentration of the unbound drug, not the overall concentration, determines the pharmacological reaction of a drug. To varying degrees, all medications bind to proteins in the blood and tissues. Extensive binding to plasma can extend biological half-life, hence protein binding is an important factor in a drug's therapeutic impact regardless of the dosage form. So, a sustained-release medication delivery mechanism isn't always necessary for this class of drugs. [35]

Margin of safety:

As we know larger the value oftherapeutic index safer is the drug. Drugs with less the rapeuticindexusuallypoorcandidateforformulation of oral SR drug delivery system [35]

Physicochemical Factors Influencing Release from Matrix Tablet

Dose size:

In systems that are meant to be taken orally, there is a maximum allowable dose size. For a traditional dosage form, the typical maximum dose is between half a milligram and one gramme. For sustained-release dose forms, the same is true. [35]

Partition Coefficient:

A medication must pass through a number of biological membranes when it is given to the GI tract in order to have a therapeutic effect elsewhere in the body. It's common knowledge that these membranes are lipidic, so an essential factor in assessing the efficacy of oil-soluble medications is their partition coefficient. [36]

Stability:

Drugs taken orally may be degraded by enzymes or hydrolyzed by acids and bases. For problem cases, the preferred composition of delivery is in a solid state since drugs in this state will degrade more slowly. Systems that extend delivery throughout the entire GI tract's transit are advantageous for dosage forms that are unstable in the stomach; this also applies to systems that postpone release until the dosage form reaches the small intestine. When given in a sustaining dosage form, compounds that are unstable in the small intestine may exhibit decreased bioavailability. This is due to the fact that more medication is absorbed in the small intestine, where it is subsequently metabolized. Examples of such drugs are propantheline and probanthine. [37-40]

Conclusion:

It is simple to conclude that sustained-release formulations, when given at a sustained dosage as discussed above, help to improve both the patient's compatibility and the dose's efficiency. Additionally, each of these is reasonably priced. For antibiotics, where excessive use could lead to resistance, the dosage form is highly beneficial and simple to adjust.

Consent for Publication

All the author approved the manuscript for Publication.

Availability of data material

All required data is available.

Conflicts of interest

The authors have declared no conflicts of interest.

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