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Research Article

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OVERVIEW OF MATRIX TABLETS

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ABSTRACT

By optimizing the bio-pharmaceutics, pharmacokinetics, and pharmacodynamic properties of drugs in a way that reduces the dosing frequency to the point where a single daily dose is sufficient for penetration, polymer swelling, drug dissolution, drug diffusion, and matrix erosion, oral sustained release (SR) products offer an advantage over conventional dosage forms. It has never been easy for pharmaceutical technologists to create an oral sustained-release matrix tablet with a constant release rate. If a medication is not properly prepared, the majority of them have the potential to release the active ingredient more quickly and to produce hazardous concentrations when taken orally. As a preferred product and crucial component for creating formulations with sustained release, hydrophilic polymers.

Keywords: Matrix system, Controlled drug delivery, Polymers.

INTRODUCTION

These are a particular kind of controlled drug delivery system that releases the drug continuously through processes that control both diffusion and dissolution. The medications are disseminated in swellable hydrophilic substances, an insoluble matrix of stiff non-swellable hydrophobic materials, or plastic materials to manage the release of the drugs, which have different solubility qualities.

To create a tablet where the medicine is embedded in a retardant matrix, a combination of drug, retardant material, and additives is directly compressed. This is one of the simplest methods for creating sustained-release dosage forms. An alternative would be to granulate the medication and retardant blend before compression. In creating matrix systems, hydrophilic and hydrophobic polymers are the most often utilized components. Hydroxanthan gum, Sodium Alginate, Poly (Ethylene Oxide), Hydroxypropyl methylcellulose (HPMC), Hydroxypropyl Cellulose (HPC), Hydroxyethyl Cellulose (HEC), and cross-linked Homopolymers and Copolymers of Acrylic acid are examples of commonly available hydrophilic polymers. Because of the importance of small particle size in the quick creation of the gelatinous layer on the tablet surface, it is typically supplied in micronized forms.

The development of matrix tablets as Sustained Release (SR) has resulted in a new advancement in pharmaceutical technology for Novel Drug Delivery Systems (NDDS). Complex production processes like coating and pelletization during manufacture are not included, and the kind and amount of polymer employed in the preparations primarily controls the drug release rate from the dosage form. A hydrophilic polymer matrix is frequently utilized to formulate SR dosage forms.

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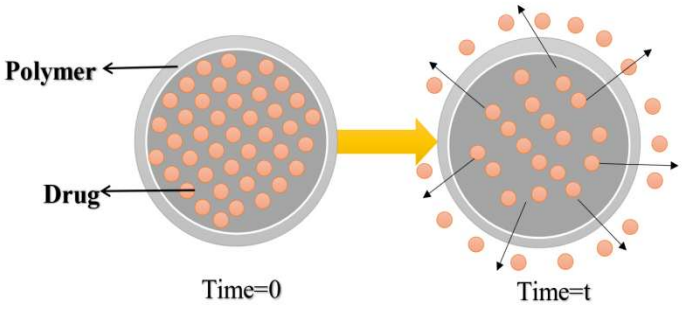

Fig.1. Drug release rate from Matrix tablet

Advantages of matrix tablet

The merits of matrix systems are as follows:

- A rise in the effectiveness of treatment.
- Affordable, practical, and adaptable.
- By delaying the absorption of the medicine, lessen its toxicity.
- By shielding the medication from hydrolysis or other derivative changes in the gastrointestinal system, you can increase its stability.
- By using sustained-release formulations, elevated blood concentrations are prevented.
- Capable of releasing molecules with a high molecular weight.
- Formulations with sustained release may increase patient compliance.
- Reduce medication build up by using continuous dosage.
- Reduce the adverse effects, both systemic and local.
- Simple to produce.
- Therapeutic concentrations may be sustained for extended periods by the sustained-release formulations.

Disadvantages of matrix tablet

The pitfalls of matrix systems are as follows:

- Boost the first-pass metabolism's potential.
- Less room for dose modification.
- Likelihood of dosage dumping.
- Lower systemic availability as compared to standard dosage forms with quick release.
- Single units are more expensive than traditional dose forms.
- Weak connection between in vitro and in vivo.

Classification of matrix tablet Based on retardant material Hydrophobic matrices

It was first proposed in 1959 to use hydrophobic or inert material as a matrix tablet. This method involves mixing the drug with an inert or hydrophobic polymer and compressing the mixture into a tablet to achieve a prolonged release from an oral dosage form.

The dissolving medication diffuses through a network of channels that are present between the particles of compressed polymer, resulting in sustained release. Although insoluble polymers have been utilized, this is the sole method where polymer use is not required to enable regulated drug release. As the name implies, the main elements of the hydrophobic matrix that regulate the rate are water-insoluble substances, like waxes, fatty acids, glycerides, and polymeric compounds like methyl and ethyl cellulose.

Matrix lipids

Lipid waxes and associated components are used to prepare these matrices. Such a substance releases drugs via pore diffusion as well as erosion. Therefore, the nature of the digestive fluid has a greater influence on release characteristics than the completely insoluble polymer matrix.

Hydrophilic matrix tablets

One of the most intriguing drug delivery methods available today is the hydrophilic matrix system. Because of their cost-effectiveness, general regulatory acceptability, and flexibility in achieving a desired drug release profile, they are most frequently employed to control the release rate of pharmaceuticals. Uniform dispersion of medication molecules inside a hydrophilic polymer skeleton that expands upon touches, such as carbopol, sodium alginate, xanthan gum, polyethylene oxide, or cellulose derivatives is one definition of hydrophilic matrix tablets. Swellable-controlled release systems are the name given to these systems. It's possible that the release rate that was seen was the zero-order release. By compression, the majority of commercial hydrophilic matrices are produced. As a result, the fundamental steps required to make the matrices are the same as those required to prepare traditional tablets. Three groups of polymers are employed in the creation of hydrophilic matrices.

- Cellulose derivatives: Sodium Carboxy methylcellulose, Hydroxyethyl Cellulose, Hydroxypropyl methylcellulose (Hpmc) 25, 100, 4000, and 15000cps, and Methylcellulose 400 And 4000cps.
- Natural or semi-synthetic non-cellulose polymers, such as modified Starches, Chitosan, Alginates, Molasses, Carbo Gum, and Polysaccharides Containing Mannose and Galactose.
- Acryl acid polymers: Carbopol 934.

Based on the porosity of the matrix Macro porous Systems

In these systems, drug diffusion takes place through matrix pores, which range in size from 0.1 to 1µm. The size of this pore exceeds that of the diffusing molecules.

Micro porous System

In this kind of system, diffusion mostly takes place through pores. For micro porous systems, pore size ranges between 50 – 200 A°, which is slightly larger than diffusing molecule size.

Polymers utilized in matrix tablets

Natural gums are nontoxic and biodegradable, and they expand and hydrate when they come into contact with aqueous media. These days, matrix tablets are frequently prepared using natural gums.
Depending on the needed type of drug release and the physicochemical characteristics of the drug component to be included in the matrix system, a variety of polymers can be employed to make matrix tablets.

Classification of sustained release drug delivery system Diffusion-controlled release systems

In these systems, the diffusion of the dissolved medication across a polymeric barrier is the rate-limiting step. The drug release rate is never zero-order because the diffusional path length grows over time as the drug is gradually removed from the insoluble matrix. The basis of controlled drug delivery systems is the drug molecule's diffusion via a polymeric membrane.

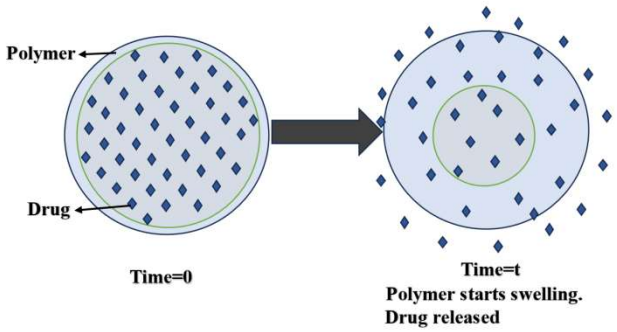

Fig.2. Diffusion-controlled release systems

Dissolution-controlled release systems

One way to accomplish dissolution-controlled release is to slow down the rate at which a drug dissolves in the gastrointestinal (GI) medium, incorporate the drug into an insoluble polymer, and coat drug particles or granules with polymeric components that vary in thickness. Diffusion across the aqueous boundary layer is the rate-limiting phase in the dissolution of a medication. The stagnant-fluid diffusional boundary layer opposes the energy source for drug release, which is provided by the solubility of the material.

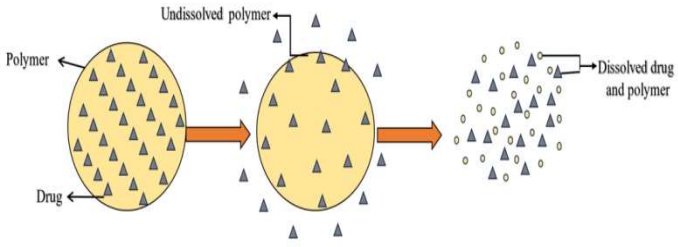

Fig.3. Dissolution-controlled release systems

Dissolution and diffusion-controlled release systems

In these systems, a partly soluble membrane surrounds the drug centre. When portions of the membrane dissolve, pores are created that enable the diffusion of the dissolved drug out of the system and the entry of an aqueous medium into the center, leading to drug dissolution.

Ion exchange resin-drug complexes

It is predicated on the creation of a drug-resin complex, which is created when ionic resins and an ionic solution interact. This complex uses an insoluble cross-linked polymer resin, which is exchanged in the gastrointestinal tract and released most of the time when an excess of Na+ and Cl is present. They have a repeating polymer chain with a salt-forming function group.

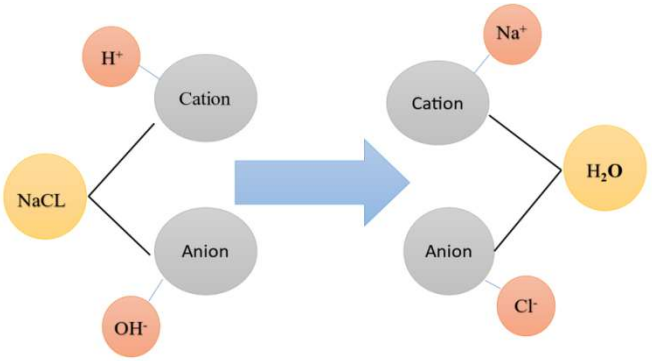

Fig.4. Ion exchange resin-drug complexes

pH-independent formulation

The release of most medications from sustained-release formulations is pH-dependent because most medicines are weak acids or bases. To help maintain a steady pH, a buffer, such as tartaric acid, amino acid, or citric acid salt, can be added to the formulation. This will delay the release of the medicine, which is reliant on pH. A buffer retain release formulation is created by combining a simple or acidic medication with one or more buffering agents, granulating with adequate excipients, and covering with gastrointestinal fluid permeability film-forming polymer. The buffering agent modifies the pH of the fluid inside the gastrointestinal tract as it travels across the membrane, causing a consistent rate of drug absorption release.

Osmotic pressure controlled systems.

The tablet, particle, or drug solution is surrounded by a semi permeable membrane that lets water in and finally pumps the drug solution out through a tiny delivery hole in the middle of the tablet.
There are two different kinds of osmotic pressure-controlled systems:

A. Type 1 has an osmotic core when using medication.
B. Type 2 uses a flexible bag with an osmotic core to enclose the medication.

An osmotic system that delivers a range of medications at a set pace can be created by optimizing the formulation and processing parameters.

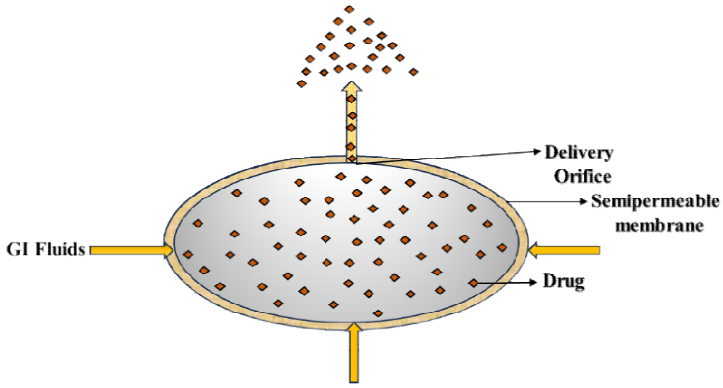

Fig.5. Osmotic pressure controlled systems.

APPROACHES FOR PREPARATION OF MATRIX TABLETS

Direct Compression (DC)

Powdered materials are immediately crushed in this method, keeping the drug's chemical and physical characteristics intact.

Wet Granulation (WG)

This process involves mixing an adequate proportion of granulating agents with weighed amounts of both the medication and the polymer. Screening of wet bulk came next, once sufficient cohesion was achieved. A single-punch tablet compression machine is used to compress the dry, screened granules, which are then combined with lubricant and disintegrant to create "running powder" tablets.

Melt Granulation

This method makes use of a material that melts at a cool temperature. When the substrate is heated above its melting point, this material can be poured on top of it in a molten state. Which are experimented with various lipophilic binders utilizing the melt granulation process.

Hot-Melt Extrusion Process

A combination of thermoplastic polymers, active substances, and other processing aids is fed through the hopper into the extruder's barrel during the hot melt extrusion process. A spinning screw moves the materials into the heated barrel. At high temperatures, the materials melt, and the molten mass is continually fed through the die that is fastened to the barrel's end. Films can also be made from the extruder, depending on the size of the die cylinders.

RECOMMENDATIONS

1. Formulation Optimization

- **Adopt Quality by Design (QbD):** Move away from "trial and error." Use **Design of Experiments (DoE)** (like Central Composite or Box-Behnken designs) to systematically study how polymer concentration and compression force affect drug release.
- **Utilize Polymer Blends:** Instead of using a single polymer (like HPMC), recommend using **synergistic blends** (e.g., HPMC with Carbopol or Sodium Alginate) to achieve more linear, zero-order release kinetics.

- **Address the "Burst Effect":** To prevent initial over-dosing, recommend using **multilayered tablets** where the outer layers are drug-free "barrier layers" that control initial hydration.

2. Advanced Manufacturing Techniques

- **Explore 3D Printing:** Recommend 3D printing (Fused Deposition Modeling) for personalized medicine, allowing for complex internal geometries that can precisely control the release surface area.
- **Hot-Melt Extrusion (HME):** For poorly soluble drugs, HME should be recommended to create solid dispersions within the matrix, improving both solubility and release consistency.
- **Sintering Processes:** Use thermal treatment (sintering) of plastic or lipid matrices to strengthen the polymer network and further retard the release of highly soluble drugs.

3. Analytical & Predictive Tools

- **Improve IVIVC:** There is a need for better **In-Vitro In-Vivo Correlation**. Recommend using biorelevant dissolution media (e.g., FaSSIF/FeSSIF) rather than simple buffers to better predict how the tablet will behave in the human stomach.
- **Incorporate AI and Machine Learning:** Recommend using **Artificial Neural Networks (ANN)** to predict dissolution profiles based on the physical properties of the API and polymers, saving time in the lab.

4. Safety & Compliance

- **Dose Dumping Protection:** Formulations should be tested for **alcohol-induced dose dumping**, especially for hydrophobic matrices, to ensure safety if consumed with certain beverages.
- **Patient-Centric Design:** For pediatric or geriatric patients, recommend the development of **mini-matrix tablets** (multiparticulate systems) which are easier to swallow and offer more flexible dosing than large monolithic tablets.

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CONCLUSION

In summary, matrix tablets represent one of the most effective and widely utilized strategies for achieving controlled drug release. By dispersing the active pharmaceutical ingredient (API) within a swellable or non-erodible polymer network, these systems provide a consistent therapeutic effect while minimizing the frequency of dosing. While challenges such as the "burst effect" and the influence of food on release rates remain, ongoing advancements in polymer science and 3D printing are further refining the precision of these dosage forms. Ultimately, the matrix system remains a gold standard in pharmaceutical technology due to its manufacturing efficiency and proven patient compliance.

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