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Review paper

A Review on Sustained Release Matrix Tablet: A Recent Approach for Oral Drug Delivery System

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ABSTRACT

Sustained release formulations are advanced drug delivery systems designed to release active pharmaceutical ingredients (APIs) over an extended period, maintaining therapeutic levels and reducing dosing frequency. These formulations enhance patient compliance, reduce side effects, and improve bioavailability. This review explores recent advancements in sustained release technologies, including Matrix systems, Reservoir systems, Microencapsulation, Nanoparticles, and Liposomes. Factors influencing drug release, such as polymer degradation, diffusion, and erosion, are discussed. Applications in various therapeutic areas, including chronic pain management, antihypertensives, and HIV treatment, are highlighted. Challenges and future directions in sustained release formulation development are also addressed.

1. Introduction

The objective of any drug delivery system is to promptly deliver a therapeutic dose of medication to a designated location inside the body and then sustain the proper drug concentration [1, 2]. Sustained release is a pharmacological formulation or delivery strategy that progressively releases a medication over time [3, 4, 5]. A matrix tablet, which includes a solid medication spread in an insoluble matrix, may allow for longer drug delivery. The medication in the bathing solution-exposed outer layer dissolves first and then diffuses out of the matrix. The rate of drug release is dictated by the rate of drug diffusion, not the rate of solid breakdown [1, 2].

Sustain-release matrix tablets are an essential instrument in current pharmaceutical science. They serve the objective of maintaining consistent medication levels in the circulation, optimising treatment results, and increasing patient compliance. The concept is based on a matrix system in which the

active component is equally distributed throughout a solid or semi-solid matrix. This matrix slows the release of the medication, resulting in regulated and sustained administration [1, 6].

2. Drugs not suited for sustained release tablets [7, 8, 9]

a) Riboflavin and ferrous salt are not well-absorbed in the lower intestine.
b) Having a short biological half-life (<1 hour), such as Penicillin G .
c) Diazepam and phenytoin have a long biological half-life (>12 hours).
d) Sulphonamide requires a large dosage (>1 gm).
e) Cumulative action and favourable side effects with a low therapeutic index, such as digitoxin.

3. Classification of Matrix Tablets Based on the retardant materials used:[3]

3.1 Hydrophilic Matrices

A hydrophilic polymer is utilised to properly incorporate one or more drugs into a matrix (gelling agent). Water-loving polymer matrices are widely used in oral controlled drug delivery due to their efficacy in producing the required drug release profile, low cost, and widespread regulatory acceptability. These matrices are divided into three kinds based on the polymer materials used[3, 10]

Cellulose derivatives: HPMC 25, 100, 4000, 15000 cps, sodium carboxymethyl cellulose, and methylcellulose 400 and 4000 cps.

Non-cellulose natural or semi-synthetic polymers: agar-agar, carob gum, alginates, polysaccharides containing mannose and galactose, chitosan, and modified starches.

Acrylic acid polymer: Carbopol-934 is the most widely used acrylic acid polymer in this category. Other hydrophilic materials used to make matrix tablets include alginic acid, gelatin, and natural gums.

Hydrophobic matrices: Plastic matrices are tablets where the active medication is compressed with plastic components to form a porous structure. Materials used as inert or hydrophobic matrices include polyethylene, polyvinyl chloride, ethyl cellulose, and acrylate polymers copolymer. [3,11]

Lipid matrix : Lipid matrix are made by combining lipid waxes and other related compounds. Such materials enable drug release by erosion and pore diffusion. Carnauba wax, along with stearyl alcohol or stearic acid, has been used as a retardant basis for many years formulations with continuous release[3,12].

Biodegradable matrices: These polymers are made up of monomers connected by functional groups with unstable backbone linkages. Natural polymers include proteins, polysaccharides, modified polymers, and synthetic polymers such aliphatic esters and poly anhydrides.[3,13].

3.2 Based on the porosity of the matrix

Macro porus system : In macro-porous systems, medicines diffuse via holes in the matrix ranging from 0.1 to 1 μm.

Micro-porous system: Diffusion in this sort of system is mostly through pores. Microporous systems have pore sizes ranging from 50 to 200 A°, which are somewhat bigger than diffusion molecules [3,14]

Non-porus System : Non-porous systems lack pores. Molecular diffusion occurs across network meshes. When the polymeric phase is present, there is no pore phase.

4. Advantages of sustain release tablet [3,13,14]

- Matrix tablets provide formulation versatility by including several excipients and polymers to produce desired release profiles.
- Increase the bioavailability of certain medicines.
- Reduces toxicity by decreasing medication absorption.
- Improves stability by preventing hydrolysis and derivative alterations in the gastrointestinal system.
- Using formulations with prolonged release helps prevent excessive blood concentration.
- Improved therapeutic effectiveness.
- Minimise local and systemic side effects.
- Consistent formulation, reduced dosing frequency, and improved patient compliance.

5. Disadvantages of sustain release tablet [17,18]

Drawbacks of Sustained Release Matrix Tablets include the need to remove the remaining matrix once the drug is released. High cost of planning. Release rates are influenced by stomach transit and other factors, such as meal intake. The square root of time affects drug release rates.

6. Formulation Process of Matrix Tablet [19, 20,21]

6.1 Wet Granulation Technique

The excipients are ground and gravity blended with polymer and drug to create a binder combination
↓
Wet massing involves adding a granulating or binder solutions
↓
Filtration of damp materials
↓
Wet grains are dried, and dry granules are screened
↓

Using an emollient to dissolve and mix to generate running powder
↓
The pill had been compacted

6.2 Dry Granulation Method

Grinding and gravitational stirring of excipients
↓
Polymer and medicines
↓
Slug or roll compaction Grinding and screening compressed powders and slugs
↓
The pill disintegrates once the lubricant is mixed and crushed

6.3 Sintering Method

Sintering is the process by which neighbouring particle surfaces combine to form a powdery mass. Traditionally, sintering involves heating solid materials to a lower temperature. Sintering has been shown to affect tablet disintegration duration and hardness at high temperatures. Sintering produces prolonged release matrix tablets that delay medicine release.

7. Factors affecting sustained-release tablets

7.1 Physiochemical Factors

1. **Dose size:** The maximum dose for sustained release formulations is 0.5-1g. Compounds with large dosage sizes can be administered in several doses or incorporated into liquid systems.[7,22]
2. **Ionization:** pKa, and water solubility Drugs are often weak acids or bases that need to remain unaltered to penetrate lipid membranes. Therefore, the pKa of the medicine is crucial. Drug solubility in watery media impacts delivery strategies based on diffusion or dissolution.[7,23]
3. **Partition coefficient:** To provide therapeutic effects, the medicine must pass biological membranes. Lipophilic drugs have a high partition coefficient, making them difficult to dissolve in water and slowing their absorption into tissues. It's challenging to pass through lipid membranes in order to deliver medications with low partition coefficients that have low bioavailability. The drug's partitioning properties .influence the choice of diffusion-limiting membranes .[7,24]
4. **Consistency :** Both hydrolysis and enzymatic degradation are applied to drugs that are taken orally. Low bioavailability occurs when compounds that are unstable in the small intestine are given in sustaining dosage forms [7,25].

7.2 Factors related to biology

5. **Absorption:** The drug's release rate needs to be lower than its absorption rate. Sustained release preparation may be detrimental if a medication is absorbed by active transport or travels to a particular area of the intestine [7,26].
6. **The Metabolism :** The medication metabolism occurs prior to absorption, which reduces the drug's bioavailability. Drug release occurs more slowly, and there is less drug metabolism prior to absorption [7,8].
7. **Half-life in biology:** A needs to have a short half-life in order to be a good fit for sustained release .[7,27]
8. **Safety margin:** Formulations for sustained release are appropriate for drugs with a high therapeutic index [7,27].

7.3 Factors pertaining to polymers

9. **Type of polymer :** The drug's release from the matrix is greatly influenced by the type of polymer used. There are two types of polymers used in the creation of extended release matrices: water-soluble and water-insoluble polymers.[28,29]
10. **Grade of polymer viscosity :** The performance of the matrix is controlled by the viscosity of the polymer chosen at a fixed polymer level, which influences the mechanical and diffusional properties of the gel layer. Higher viscosity grade polymers form a mechanically stable gel layer quickly after hydrating. Rapid gel development is exhibited by fast-hydrating polymers, which limits initial dose dumping from a matrix and prolongs the release time.[28,30,31]
11. **Polymer percentage :**Changing the level of polymers in the matrix system can alter the medication release profile. Increasing the polymer level raises the gel layer's viscosity, leading to longer diffusion paths. Lowering the diffusion co-efficient of a medication may lead to reduced release.[28,32]
12. **Polymer particle characteristics:** It was discovered that decreasing particle size resulted in a weaker burst effect and increased lag times. The gel barrier was quickly established due to the faster swelling of smaller particles, as explained.[28,33]
13. **Polymer blend :** Drug release from matrix tablets may be synergistically delayed by a combination of polymers. The molecular physical interaction between the individual polymers could be the cause of this synergism.[28,34]

7.4 Factors connected to formulation

14. **Formulation geometry** (Tablet size and shape)**:** The rate of drug dissolution can be influenced by the dimensions and form of a tablet designed as a matrix system that exhibits erosional as well as diffusional release. To achieve the lowest release rate possible for a given tablet shape, tablet matrices should be produced as spherical as possible.[28,35]
15. **Process variables :** According to reports, formulations created using the direct compression technique released metoprolol tartrate more quickly than formulations created using the fluid-bed and high-shear granulation techniques. The hardness and thickness of the tablets are greatly affected by increasing the compression force.[28,32]
16. **Additives for Formulation:** Because these interactions may have an impact on the release and bioavailability of the drug, preformulation studies of potential interactions between excipients in the solid dosage forms are required.By shortening the diffusional path length, soluble fillers facilitate the dissolution of soluble drugs, whereas insoluble fillers impede the diffusion rate by obstructing the tablet's surface pores.[28,36]

8. Evaluation of sustain release matrix tablet [25, 37, 38]

A product's strength, safety, stability, and dependability must be ensured before a sustained release product is marketed by developing an in-vitro and in vivo study and a correlation between the two. Numerous writers have covered the evaluation criteria and methods for tablets with extended release.

1) **Weight Variation:** After weighing each of the twenty pills separately, the average weight of the tablets was determined.
2) **Hardness:** Hardness test was done for tablets from each batch using Monsanto hardness tester and average results were determined.
3) **Friability:** The Roche friabilator, which spins at 25 rpm for four minutes, was used to assess the tablets' friability
4) **Thickness :** Tablet thicknesses were determined using a micrometre screw gauge.
5) **Content uniformity:** To determine drug content uniformity, use a UV Visible spectrophotometer and the calibration curve technique.
6) **Swelling Index:** [3] Weight growth was used to study a dosage unit's swelling behaviour (Swelling Index). Tablet swelling index was measured in a petri dish using 0.1N HCL (pH 1.2) and pH 7.4 phosphate buffer.

9. Conclusion

Sustained release tablets have revolutionized drug delivery, offering improved patient compliance, reduced side effects, and enhanced therapeutic efficacy. Advances in formulation techniques, materials science, and manufacturing technologies have expanded the scope of SR tablets. Despite challenges, ongoing research and innovations continue to optimize SR tablet design, ensuring Improved bioavailability and pharmacokinetic profiles. Enhanced patient adherence through reduced dosing frequency. Targeted drug delivery, minimizing systemic side effects. Personalized medicine, tailoring release profiles to individual needs. As SR tablet technology continues to evolve, it holds promise for addressing unmet medical needs, improving patient outcomes, and transforming the pharmaceutical landscape. SR tablets offer improved patient compliance and reduced side effects. Advances in formulation techniques and materials science drive innovation. Ongoing research addresses challenges, optimizing SR tablet design. Emerging technologies hold potential for personalized, targeted drug delivery.

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