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A REVIEW ON SUSTAINED RELEASE MATRIX TABLET

Payal Mohaniya*; Dipti Modi; Rajat Pawar
Swami Vivekanand College of Pharmacy Indore (M.P)
Correspondence address: payalmoahniya155@gmail.com

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ABSTRACT: In the present study Sustained release matrix tablet is formulated mainly by wet granulation or direct compression method .Sustained release drug delivery maintains the therapeutic concentration of drug in the bloodstream over a long period of time and thus improves patient compliance by reducing frequency of dosing, minimized fluctuations in drug levels, lowering the therapeutic index and improving treatment efficacy. Nowadays Matrix tablets as oral solid dosage form are most suitable for the sustained release drug delivery. In a matrix system a drug is homogeneously dispersed or dissolved within the hydrophilic or hydrophobic polymer like HPMC, PEG through various (diffusion, dissolution, ion exchange and pH dependent formulations) mechanism.

KEYWORDS: Sustained release, Matrix tablet, Polymers, hydrophobic Polymer, dissolution

1.0 INTRODUCTION

The oral route is the most popular route used for administration of drugs, which is due in part to the ease of administration and to the fact that gastrointestinal physiology offers more flexibility in dosage form design than most other routes[1,2]. Sustained release refers to a pharmaceutical formulation or drug delivery system designed to release a drug gradually over an extended period of time. The goal of sustained release is to maintain a therapeutic concentration of the drug in the bloodstream or target tissue for an extended duration, often allowing for less frequent dosing compared to immediate-release formulations. Matrix tablets are solid oral medications where the active drug is uniformly dispersed or dissolved within either hydrophilic or hydrophobic polymeric matrices. These tablets are designed to provide sustained or controlled release of the drug, ensuring consistent therapeutic levels in the bloodstream for an extended duration. Hydrophilic polymer matrices are commonly employed in these formulations due to their ability to achieve desired drug release profiles, cost-effectiveness, and widespread regulatory acceptance. The release of the drug from hydrophilic matrices involves a complex interplay of

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dissolution, diffusion, and erosion mechanisms. Matrix tablets are preferred for sustained-release formulations as they involve minimal processing variables, utilize standard manufacturing facilities, and can accommodate large drug doses. There is ongoing interest in developing innovative formulations that achieve sustained drug release using readily available and affordable excipients through matrix-based formulations.[3]

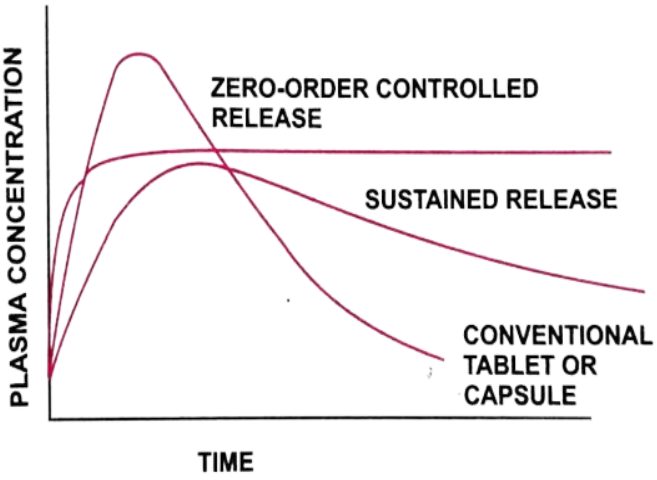

Fig.1: Plasma drug concentration vs time profile for sustained release formulation, conventional tablet or capsule formulation and zero order controlled release formulation.

2.0 ADVANTAGES OF MATRIX TABLETS[4,5]

- Matrix tablets offer flexibility in formulation design, allowing for the incorporation of various excipients and polymers to achieve the desired release profile.
- Enhance the bioavailability of certain drugs.
- Reduce the toxicity by slowing drug absorption.
- Increase the stability by protecting the drug from hydrolysis or other derivative changes in gastrointestinal tract.
- Utilizing formulations with a sustained release prevents high blood concentration.
- Improvement in treatment efficacy.
- Minimize the local and systemic side effects.
- Stable and Consistent Formulation.
- Reduced dosage frequency.
- Improved patient compliance.

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3.0 FACTORS INFLUENCING RELEASE FROM MATRIX TABLET

Biological Factors:

Biological half-life: The half-life of a drug is the measure of its time of residence in the body. If the medication has a short half-life (less than 2 hours), a prohibitively large amount of the drug may be found in the dosage form. On the other hand, a drug with a half-life of removal of eight hours or more is adequately maintained in the body when administered in traditional doses and continuous delivery of drugs systems[6, 7]

Absorption and solubility: Absorption and solubility both are interlinked and incorporation of drugs which are poorly water soluble can cause the reduction in overall absorption efficiency.

Metabolism: Drugs that are significantly metabolized before absorption, either in the lumen or the tissue of the intestine, can show decreased bioavailability from slower-releasing dosage form.

Distribution: Drugs with high apparent volume of distribution, which influence the rate of elimination of the drug, are poor candidates for oral SR drug delivery system e.g. Chloroquine.

Protein Binding: The Pharmacological response of a drug depends on unbound drug concentration rather than total concentration and all drugs are bound to some extent to plasma and or tissue proteins.

Margin of Safety: The safety of a drug is typically assessed based on its therapeutic index, where a higher value signifies a safer drug. Drugs with a narrow therapeutic index are usually not suitable for developing oral sustained-release (SR) drug delivery systems due to challenges in controlling release rates imposed by technology constraints.

Physicochemical Factors [8] :

Drug Stability: The important factor in oral dosage forms is the loss of medication in the GI tract by means of acid hydrolysis and/or metabolism. While a drug undergoes degradation in solid states at a much slower rate than a suspended or solution substance.

Aqueous solubility & pKa: A medicine that will be soaked up, dissolved, and partitioned into the absorbing membrane within a water-phase close to the administration site's route. The water solubility and, if the drug is a soft acid, the pKa of the drug are two of the most significant physicochemical characteristics that influence its absorption activities.

Partition Coefficient: It refers to how much medicine is present compared to the water phase, in the organic phase. Because they won't be leaving the phospholipid membranes through partitioning once they enter it, drugs with greater partition coefficients are not suited for oral SRDDS. By using the formula, it may be determined [9].

$K = Co / Cw$

Co = Conc. at eqm. in the oil phase.

Cw = Conc. in water phase at equilibrium

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Diffusivity and molecular size : For drugs having molecular weight >500 Daltons, the diffusion coefficient in many polymers is very less i.e. less than 10-12cm2/sec. Proteins and peptides are examples of drugs that are difficult to control drug release level from dosage form.

4.0 CLASSIFICATION OF MATRIX TABLETS

On the basis of retardants material used:

Hydrophilic Matrices:-A hydrophilic polymer is used to correctly integrate one or more medicines into a matrix (gelling agent). Due to its effectiveness in achieving a desired drug release profile, affordability, and broad regulatory acceptance, water-loving polymer matrices are frequently employed in oral controlled drug delivery. Based on the types of polymers utilized, these matrices are further categorized into three classes[10].

- **Cellulose derivatives** - HPMC 25, 100, 4000, 15000cps, sodium carboxymethyl cellulose and Methylcellulose 400 and 4000 cps.
- **Non cellulose natural or semi-synthetic polymers** -Agar-agar, carob gum, alginates, polysaccharides of mannose and galactose, chitosan and modified starches.
- **Acrylic acid polymers -** Carbopol-934 is the most frequently used polymer in this group and Other hydrophilic materials used for preparation of matrix tablets are Alginic acid, Gelatin and Natural gums.

Hydrophobic matrices (Plastic matrices):-In the hydrophobic matrix tablets, the active drug is dispersed in a tablet within a porous skeletal structure by direct compression of the drug with plastic materials. Examples of materials that have been used as inert or hydrophobic matrices include polyethylene, polyvinyl chloride, ethyl cellulose and acrylate polymers and their copolymers[11].

Lipid matrices:- Lipid waxes and other similar substances are used to create these matrices. Such materials allow for the release of drugs via erosion and pore diffusion. Carnauba wax in combination with stearyl alcohol or stearic acid has been utilized as a retardant base for many sustained release formulations[12].

Biodegradable matrices:-These consist of the polymers which consist of monomers linked to each other by functional groups and have unstable linkage in the backbone. Examples are natural polymers such as proteins, polysaccharides, modified natural polymers and synthetic polymers such as aliphatic poly (esters) and poly anhydrides.

Mineral matrices:-Mineral matrices consist of polymers which are obtained from various species of seaweeds, eg. alginic acid which is a hydrophilic carbohydrate obtained from species of brown seaweeds (Phaeophyceae) by the use of dilute alkali[13]

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On the basis of porosity of matrix:-

Macro-porous systems:- In such systems the diffusion of drugs occurs through pores of matrix which are of size range 0.1 to 1 μm.

Micro-porous system:- Diffusion in this type of system occurs essentially through pores. For micro porous systems, pore size ranges between 50 – 200 A°, which is slightly larger than diffusion molecules size[14].

Non-porous system:- No pores exist in these systems. Molecular diffusion takes place through network meshes. Where the polymeric phase is present, there is no pore phase.

5.0 MECHANISM OF DRUG RELEASE

Dissolution controlled release systems: A drug which has a slow dissolution rate these drugs are naturally sustained and for those drugs with high water solubility, decrease their dissolution rate through appropriate salt or derivative formation. These systems are generally employed in the manufacturing of enteric coated dosage forms. [15,16]

Diffusion controlled release systems: It involves the passage of drug molecules from higher concentration to the lower concentration. The flux of drug is given by

J = - D dc/dx

D = diffusion coefficient in area/ time dc/dx = change of concentration 'c' with distance 'x'

Dissolution and diffusion controlled release systems: In such systems, the drug core is encased in a partially soluble membrane. Pores are thus created due to dissolution of parts of the membrane which permit entry of aqueous medium into the core and hence drug dissolution and allow diffusion of dissolved drug out of the system.

Ion exchange resin- drug complexes: Ion exchange based delivery systems represent a better approach for a drug that is highly susceptible to degradation by enzymatic processes. In tablet formulations, ion exchange resins have been used as disintegrants, because of their swelling ability. Ion exchange resin which are divided into types:

a) Cation exchange resin

b) Anion exchange resin

pH– Independent formulations: Maintain the constant pH , help to make pH independent drug release substitutes such as amino acid salts, citric acid, phthalic acid, phosphoric acid and tartaric acid applied to the formulation.

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6.0 POLYMERS USED IN MATRIX TABLETS[17]

Hydrogel- polyethylene oxide (PEO), cross-linked polyvinyl pyrrolidone (PVP), Polyvinyl alcohol (PVA), Polyhydroxyethyl methyl acrylate.

Soluble polymers- PEG, PVA, PVP, and HPMC.

Biologically based polymers - PGA, PCL, polyanhydrides are examples of polymers.

Non-biodegradable polymers - Cellulose acetate (CA), Polyvinyl chloride (PVC), Polyether urethane (PEU), Polydimethylsiloxane (PDS), Polyethylene vinyl acetate (PVA), and Ethylcellulose (EC).

Mucoadhesive polymers - SCMC, tragacanth.

Natural gums - Xanthan gum, guar gum, locust bean gum and acacia.

There are some natural polymers which have been recently used in Matrix tablets as release modifiers eg.Tamarind Seed Gum, Fenugreek Seed Gum Hibiscus mucilage etc.[18]

7.0 EVALUATION TEST FOR SUSTAINED RELEASE MATRIX TABLET[19]

Weight Variation:- 20 tablets from the formulated batch were individually weighed using an electronic balance, and their average weight was determined.

Hardness:- Hardness test was conducted for tablets from each batch using Monsanto hardness tester then average values were calculated.

Friability:- The friability of the matrix tablets was measured by a Roche Friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. Permitted friability limit is 1 % w/w

Thickness:- Tablet thickness was measured using a Vernier Caliper. For this 5 tablets from each batch were measured for thickness, and the mean thickness was calculated.

Drug Content:- It was calculated by using UV Visible Spectrophotometer.

In-vitro dissolution study:- Drug release generally determined in Rotating paddle apparatus and mainly buffer is used as dissolution medium.

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