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A REVIEW ON SUSTAINED RELEASE MATRIX TABLET

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ABSTRACT:

The advantages of using a single dose of an over-the-counter medication instead of multiple dosages are now the day of interest for practicing scientists in the pharmaceutical industry. With most medicines. The basic goal of treatment is to achieve a stable blood level or a level that is medically effective and non-toxic. The continuous release system is considered a smart drug that is short-lived and requires repeated dosing, is easy to form and does not care about the process of absorption in the intestinal tract after oral administration. The main reason for the continued release of the drug delivery system is to improve the biopharmaceutical, pharmacokinetic and pharmacokinetic properties of the drug in such a way that its use is improved, side effects are reduced and treatment of disease is achieved. There are a few benefits of continuous drug delivery (matrix) in addition to standard dosage forms such as improved patient compliance due to regular drug administration, reduced flexibility in drug levels in severe conditions, higher drug use, increased dosage of strong drug safety, improved continuous oral matrix tablet with continuous dose it was a challenge for a medical professional. Many drugs, if not properly formulated, can release the drug very quickly, and may produce toxic effects of the drug in oral administration.

KEY WORDS: Sustained release, Matrix system, Extended Period of time, short half-life, pharmacokinetic, pharmacodynamics

INTRODUCTION:

A number of words have been used to describe oral volume forms representing modified release structures; which includes delayed release, repetitive action, long-term release, continuous release, extended release and controlled release. Each drug delivery program focuses on eliminating circulating changes in plasma drug concentrations seen after the administration of conventional delivery systems. Adjusted dosage dosage forms are designed to provide immediate success of the plasma level of a drug that remains unchanged in the duration of the drug treatment period over a significant period or the gain of low-dose plasma concentration (i.e. continuous release) lasting between the duration of treatment. (1)

Based on the assumption that the drug, which will be included in a modified dosage release form, provides the physical features of an open-commissioned single model, then the basic kinetic design of such a product can be assumed to consist of two components, one providing the initial loading capacity, and one that will provide adjustment or continuous volume. To ensure that the concentration of the drug in the body remains unchanged, two conditions must be met, namely 1) The zero level of drug release should determine the level of drug absorption, and 2) The dose at which the drug is available. extracted from the dose of care (and subsequently the absorption rate) should be commensurate with the level of drug elimination in the concentration area required list of key words describing the various modified release dosage forms described below. (2)

1. **Modified Release:** These dosage forms its dosage and / or drug dosage features are selected for therapeutic and / or simple purposes that are not provided for standard dosage forms. (3)

2. **Controlled Release:** The drug is dispensed at a fixed rate (zero order) and the dosage of the drug obtained after treatment does not change over time. (4)

3. **Release is delayed:** The drug is released at a later time after treatment. (5)

4. **Extended release:** Slow release of the drug for plasma concentrations is maintained at a long-term treatment level usually between 8 and 12 hours. (6)

5. **Long-term release:** The drug is provided for longer duration than normal dosage. However, there is a sense in which the onset is delayed due to the slow rate of release as a whole in the form of doses. (7)

6. **Repeat the action:** Indicates that each dose is discharged appropriately immediately after administration, and that the second dose is administered at a later time. (8)

7. **Continuous release:** The drug is gradually released at a rate controlled by the delivery system.

Oral Sustained Release Release Form:

Stable release, continuous action, extended action, controlled release, extended action, depot words used to identify drug delivery systems are designed to achieve a long-term therapeutic effect by continuing drug delivery over time after single dose administration. In the case of oral administration this time is measured in hours and in the case of injections this time varies from days to months. Several parameters should be remembered before forming a continuous release rate formula that includes different pH in the GIT, intestinal flow, enzyme system and its effect on dose and drug form. Most dosage form for continuous release follows the method of distribution, dispersion or combination of both, to produce a slow release of the drug at a predetermined rate. Considered, the dosage form for continuous release should release the drug in the form of a random order that keeps the plasma level of the drug similar to intravenous injection. Plasma drug concentration- profiles for normal tablet or capsule formation profiles, continuous release formation, and continuous zero release formation are as follows in Figure 1 provided. (9)

Benefits of Sustain Release Dosage Forms: (10)

1. Drug treatment control is achieved.
2. The level and level of drug absorption can be changed
3. The frequency of drug administration decreases.
4. Patient compliance can be improved.
5. Drug administration can be made easier
6. Increase drug availability in small doses.
7. The safety limit for a highly potent drug may increase.

Disadvantages of sustained release dosage forms: -

1. It does not allow for immediate termination of treatment.
2. Slight variability in volume adjustment.
3. These dosage forms are designed on the basis of a half-life of biological life.
4. They are expensive.

Selection of Drugs for the Oral Drug Delivery Program:

The biopharmaceutical evaluation of a drug that may be used in a controlled drug delivery system requires information on how to absorb the form of the G-form drug. I., normal absorption, drug molecular weight, pKa, melting at different pH and apparent partition coefficient.. [(11)]

Table 1: Parameter for Drug Selection

Parameters	Preferred Value
Molecular Weight/Size	< 1000
Solubility	> 0.1 µg/ml for pH 1 to 7.8
Pk_a	Non ionized moiety > 0.1% at pH 1 to 7.8
Apparent Partition Coefficient	High
Absorption Mechanism	Diffusion
Absorbability	From all G.I. segments
Release	Should not be influenced by pH and Enzyme

Table 2: Pharmacokinetic parameter for drug selection

Parameter	Preferred Value
Elimination half life	Preferably between 0.5 and 8h
Total clearance	Should not be dose dependent
Elimination rate constant	Required for design
Apparent volume of distribution Vd	The larger Vd and MEC, the larger will be the required dose size.
Absolute bioavailability	Should be 75% or more
Intrinsic absorption rate	Must be greater than release rate
Therapeutic concentration Cssav	The lower Cssav and smaller Vd, the loss among of drug required
Toxic concentration	Apart the values of MTC and MEC, safer the dosage form. Also suitable for drugs with very short half-life.

Classification of SR Formulation:

The methods used to achieve sustained release of orally administered drugs delivery systems are as follows: [12]

- Diffusion System
  - Reservoir Device
  - Matrix Device
- Dissolution System
- Osmotic System
- Ion-exchange Resin
- Swelling and Expansion System
- Floating System
- Bioadhesive or Bucoadhesive or Mucoadhesive system

Matrix System: [13]

The matrix device, as the name implies, contains a substance dispersed in the same manner throughout the polymer matrix. In the model, the outer layer exposed to the bath solution dissolves first and then disperses out of the matrix. This process continues with the interface between the solvent solution and the solvent-soluble solution, apparently, in order for the system to control the dispersion, the rate of dissolution of the drug particles within the matrix must be too fast for the dispersal to consume the dissolved drug leaving the matrix.

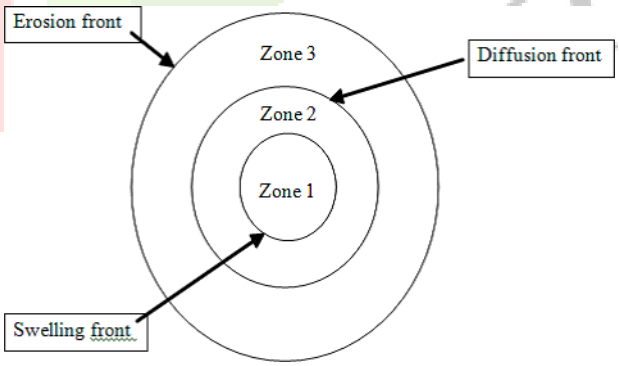

Fig 1: Sustain Release Matrix System

Advantages of Matrix system: (14)

1) Maintains long-term therapeutic focus.

2) It avoids high blood pressure.

3) Reduce toxicity by reducing drug absorption.

4) Minimize local and system side effects.

5) Improving treatment success.

6) Better drug use.

7) Reduce drug overdose by chronic dosing.

8) It can be done to release molecular weight compounds.

9) Enhance stability by protecting the drug from hydrolysis or other mutations in GIT.

10) Reducing the cost of health care.

11) Substantial drug use less.

12) Development of the ability to provide special results. Ex: Morning rheumatoid arthritis by using a sleeping pill.

13) Improved patient compliance.

The disadvantages of the Matrix system:

1) The remaining matrix should be removed after drug release.

2) Significant dependence on GI duration of dosage form.

3) Increased strength of first pass metabolism.

Matrix Types: [15]

• Hydrophobic Matrix

In this method of obtaining continuous release in oral dosage form, the drug is mixed with an inert or hydrophobic polymer and pressed into the tablet. Stable emissions are produced due to the dissolving solvent being distributed through a network of existing channels between the composite polymer particles. Examples of materials that have been used as inert or hydrophobic matriculants include polyethylene, polyvinyl chloride, ethyl cellulose and acrylate polymers and their copolymers.

• Lipid matrix

These matrices are prepared for lipid waxes and related substances. Drug release in such matrices occurs in both the distribution of pores and erosion. Extrusion elements are therefore more sensitive to the formation of digestive fluids than to a completely insoluble polymer matrix. Carnauba wax mixed with stearyl alcohol or stearic acid has been used as an old base in many continuous release formulations.

• Hydrophilic matricx

A matrix is defined as a well-mixed compound of one or more chemicals containing a gelling agent (hydrophilic polymer). These systems are called swellable controlled release systems. The polymers used in the preparation of hydrophilic matrices are divided into three broad groups,

• Cellulose Derivatives:

Methylcellulose 400 and 4000cPs, Hydroxy ethyl cellulose; Hydroxypropylmethylcellulose (HPMC) 25, 100, 4000 and 15000cPs; and sodium carboxymethylcellulose.

• Natural non-cellulose or semi synthetic polymers:

Agar-Agar; Carob gum; Alginates; Molasses; The polysaccharides of mannose and galactose, chitosan and modified starch.

- **Biodegradable Matrices**

These include polymers that combine monomers that are connected to each other by functional groups and that have unstable connections to the spine. It is biologically damaged or degraded by enzymes produced by surrounding living cells or by a non-enzyme process in oligomers and monomers that can be metabolized or excreted. Examples are natural polymers such as proteins and polysaccharides; natural polymers replaced; polymers produced as aliphatic poly (esters) and poly anhydrides.

• Minerals Matrices

These include polymers found in various types of seaweed. For example Alginic acid is a hydrophilic carbohydrate found in a species of brown seaweed (Phaephyceae) by the use of refined alkali. Based on the Porosity of the Matrix: Matrix tablets can be divided into 3 types.

- **Macro porous systems**

In these systems the distribution of the tree occurs through the holes of the matrix, which range in size from 0.1 to 1 μm. This hole size is larger than the size of the separated molecule.

• Micro porous system

Distribution in this type of system occurs mainly through pores. In micro porous systems, the pore size varies between 50- 200 A °, slightly larger than the size of different molecules.

- **Non porous systems**

Non-porous systems have no pores and molecules are scattered across network networks. In this case, only a polymeric phase is present and no pore phase is present.

Methods of preparation [16]

Direct Compression

In this process first powder is blended or mixed and powdered materials are compressed directly without changing the properties of the drug like physical and chemical properties.

Wet Granulation

In this method the measured mass of drug and excipients is mixed with a sufficient volume of granulating agent. After sufficient solidification is obtained, the wet weight is considered. The dried granules are then tested for dry granules, and then mixed with lubricant and disintegrant to produce compressed "running powder" tablets using a single punch tablet compressor.

Melt Granulation

In this process the use of the substance, which melts at low temperatures. This substance can be added by dissolving it over the substrate, which is then heated above its melting point. Different lipophilic bonds were tested using a granular solution.

Hot-Melt Extrusion Process

In the process of hot-melt extrusion, a mixture of active ingredients, thermoplastic polymers and other processing materials is placed in the extruder barrel using a hopper. The materials are transferred inside the hot pipe by a rotating screw.

Soluble substances at high temperatures and the molten mass are continuously processed with an asset attached to the end of the barrel. Depending on the size of the die cylinders, films can also be produced in the extruder.

Effect of Release limiting factor on drug release [17]

- Polymer hydration:
- Drug solubility
- Solution solubility
- Polymer diffusivity
- Thickness of polymer diffusional path
- Thickness of hydrodynamic diffusion layer
- Drug loading dose
- Surface area and volume
- Diluent’s effect
- Additives

Polymers used in Matrix tablets [18,19]

a) Hydrogels

Polyhydroxyethylemethylacrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Crosslinked polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA).

b) Soluble polymers

Polyethylene glycol (PEG), polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC).

c) Biodegradable polymers

Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), Polyanhydrides, Polyorthoesters

d) Non-biodegradable polymers

Polyethylene vinyl acetate (PVA), Polydimethylsiloxane (PDS), Polyether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC)

e) Mucoadhesive polymers

Polycarbophil, Sodium carboxymethyl cellulose, Polyacrylic acid, Tragacanth, Methyl cellulose, Pectin

f) Natural polymers in sustained release drug delivery

Xanthan Gum, Guar Gum, Sodium Alginate, Pectin, Chitosan

Table 3: Different drugs and polymers used in sustained- release MATRIX tablets

Drug	Polymer
Metoclopramide Hydrochloride	Hydroxy Propyl Methyl Cellulose (HPMC), Carboxymethylcellulose (CMC), Ethyl Cellulose (EC)
Ibuprofen	Ethyl cellulose, Cellulose acetate phthallate
Metoprolol succinate	HPMC K100M, Xanthan gum
Ambroxol Hydrochloride	HPMC
Tramadol Hydrochloride	Xanthan gum, Guar gum.
Tramadol Hydrochloride	Carrageenan gum, Karaya gum, HPMC K15 .
Aceclofenac	Carbopol 971P, Carbopol

Evaluation of Sustained release Matrix tablets: [20, 21]

Before marketing a sustainable output product, you should ensure the strength, safety, stability and reliability of the product by performing in-vitro and in vivo analysis and the relationship between the two. Various authors discussed the criteria for testing and the processes for the development of continuous releases

• **Weight Variations:** Twenty pills are measured individually and combined, calculated by the average weight of the pills.

• **Hardness**: Strength tests are performed on tablets in each group using a Monsanto hardness tester and average values are calculated.

• **Friability**: Pills tested for elasticity using a Roche friabilator, around 25rpm 4min.

• Size: The size of the tablets is determined using a micrometer screw gauge.

• **Content Uniformity:** Using a visible UV spectrophotometer obtained the value of a drug using a curve measuring method.

• **Kinetic Studies**

• **In Vitro Dissolution Study:** Drug release research is usually based on the Rotating Paddles apparatus. In particular the buffer is used as a scattering point. The bath temperature is maintained at 370C and the required sample of the soluble area where the drug release is taken at normal time and then returned to the same local area. Exhaust drug values are determined using a UV spectrophotometer A drug dispersed at a specified time is a plot as a percentage release compared to time.

• Stability Studies: Short-term Stability Study: Determining the change in vitro release profile in storage, a short-term stability study for the right mass.

• **In-Vivo Methods** Once a satisfactory in-vitro profile is achieved, it becomes necessary to conduct in-vivo testing and establish in-vitro in-vivo relationships. The different methods of in-vivo testing are: -

- a. Clinical response
- b. Blood level data
- c. Urinary excretion studies
- d. Nutritional studies.
- e. Toxicity studies
- f. Radioactive tracer techniques

Conclusion:

The focus of this review article has been on the development of sustained-release matrix tablets, advantages and disadvantages and the various polymers used to design such a system. The above discussion concludes that matrix pills help to overcome patient compliance and the effectiveness of dose form in rewarding problems related to the therapeutic response related to standard dose forms. Cost performance and volume once a day combined points and other benefits. Therefore, matrix tablets released regularly tend to improve the formation of volume form.

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