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**Review Article**

# A Review on Sustained Release Matrix Tablet

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**Abstract:** Sustained release matrix tablet is formulated primarily by wet granulation or direct compression method or by dispersion of solid particle within solid particle within a porous matrix formed by using different polymers such as Poly methyl methacrylate (PMMA), Polyglycolic acid and HPMC etc. The matrix controls the release rate of drug. Release retardants such as HPMC can help in sustained release and hence they form core excipient in the formulation. The method involves the direct compression of blend of drug, retardant material and additives to formulate a tablet in which the drug is embedded in a matrix core of the retardant, alternatively granulation can be carried out prior to compression. The matrices used might be of hydrophilic, hydrophobic, mineral, or biodegradable types. The drug release rate can be studied by in-vitro dissolution studies. Sustained release matrix tablets can assure better patient compliance through reduction in total dose and dosage regimen, which can be of great help to treat chronic diseases.

**Keywords:** Sustained release, matrix tablet, dissolution studies, biodegradable polymer.



## INTRODUCTION

The purpose of any drug delivery system is to provide a therapeutic amount of drug to the specific site in the body to achieve on time and then maintain the desired drug concentration (Kumar S *et al.*, 2013). Sustain release system includes any drug delivery systems that reaches slow release of drug over a prolong period of time (Pundir S *et al.*, 2013). There remains an interest in developing novel formulations that allow for sustained the drug release using readily available, inexpensive excipient by matrix-based formulation. During the last two decades there has been remarkable increase in interest in sustained release drug delivery system. This has been due to various factors like the prohibitive cost of developing new drug entities, expiration of existing international patients, discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems. Now a day's the technology of sustained release is also being applied to veterinary products also (Jaiminiand K, 2012).

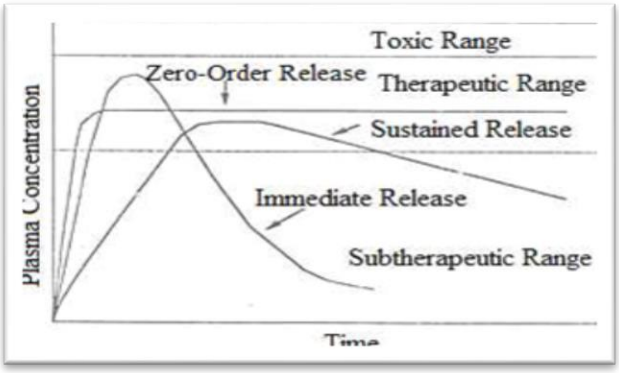


**Figure 1:** Drug level vs. time profile showing the relationship different release (Chugh I *et al.*, 2012).

**Advantages of sustained release matrix tablet:**

- Patient compliance.
- Reduced 'see-saw' fluctuation.
- Improvement of deficiency in treatment (Lieberman H et al.)

**Disadvantages of sustained release matrix tablet**

- Reduced potential for dose adjustment.
- Cost is more than conventional dosage form.
- Increase potential for first pass metabolism.
- For proper medication patient need to education is necessary.
- Possible to reduction in systemic availability.
- Dose dumping (Chauhan M, 2012).

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**Characteristics of drug unsuitable for peroral sustained release forms:**

- Not well absorbed in the lower intestine e.g. Riboflavin and Ferrous salts
- Absorbed and excreted rapidly short biological half-life (≤1hr) e.g. Penicillin G and Furosemide
- Long biologic half-life (≥12 hrs.) e.g. Diazepam and Phenytoin
- Large dose required e.g. > 1gm sulphonamide (Kumar S *et al.,* 2012).

**Criteria to be met to incorporate the drug into sustained release dosageform:**

- Physicochemical parameters for drug selection.
- Pharmacokinetic parameters for drug selection.

**Physicochemical parameters for drug selection:**

- Molecular size should be ≤ 1000 Daltons.
- Aqueous Solubility should be More than 0.1 mg/ml for pH 1 to pH 7.8
- Apparent partition coefficient should be high.
- General absorbability from all GI segments release should not be influenced by pH and enzymes (Nagarjuna T *et al.*, 2013).

**Pharmacokinetic parameters for drug selection**

- Elimination half-life of drug is in between 2 to 8 hrs.
- Absolute bioavailability Should be 75% or more
- Absorption rate constant (Ka)Necessity higher than release rate
- Apparent volume of distribution (Vd), Larger Vd and MEC, Larger will be the required dose
- Total clearance not depends on dose (Patel H *et al.*, 2011).

**Different types of Matrix tablet**

**a) Hydrophilic Matrix Tablet:** Hydrophilic matrix generally used to control the release rate of drug. The matrix can be tablet by direct compression of the blend of active ingredient and certain hydrophilic carriers or from a wet granulation containing the drug and hydrophilic matrix materials. Water is required for the hydrophilic matrix to activate the release mechanism.

**b) Fat-wax Matrix Tablet:** Various technique used for incorporation of drug into fat wax granulation which involve spray congealing in air, blend congealing in an aqueous media with or without the aid of surfactant and spray drying Technique. Mixing of active ingredients waxy materials and fillers when the mixing is over this mixture converted into granule by compacting with s compactor, heating in a suitable mixture such as fluidized-bed and steam jacketed blender or granulating with a solution of waxy material. (Patel H *et al.*, 2011).

**c) Plastic Matrix Tablet (Hydrophobic matrices):** Release is usually delayed because the dissolved drug has to diffuse through capillary network between the compacted polymer particles. Plastic matrix tablets, in which the active ingredient is embedded in a tablet with coherent and porous skeletal structure, can be easily prepared by direct compression of drug with plastic materials.

**d) Biodegradable Matrices:** These consist of the polymers which comprised of monomers linked to each other by functional groups and have unstable linkage in the backbone. It is biologically degraded or eroded by enzymes generated by surrounding living cells or by non-enzymatic process into oligomers and monomers that can be metabolized or excreted.

**e) Mineral Matrices:** Mineral matrices consist of polymers which are obtained from various species of seaweeds. Example: Alginic acid which is a hydrophilic carbohydrate obtained from species of brown seaweeds or Phaeophycean by the use of dilute alkali.

**Classification of sustained release Formulation** (Parkhi M *et al.*, 2013)

- **Diffusion sustained system:**
- **Diffusion reservoir system:**
- **Diffusion matrix type:**
- **Dissolution sustained systems:**
- **Altered density formulations:**
  - High density approach:
  - Low density approach:

**Polymers used in matrix tablet:**

**Hydrogels:** Polyhydroxyethylemethylacrylate (PHEMA), Crosslinked polyvinyl alcohol (PVA), Cross-linked polyvinyl pyrrolidone (PVP), Polyethylene-oxide (PEO), Polyacrylamide (PA) (Kant S *et al.*, 2012).

**Soluble polymers:** Polyethyleneglycol (PEG), Polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Hydroxypropyl methylcellulose (HPMC).

**Biodegradable polymers:** Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), Polyanhydrides (Aulton M *et al.*, 2005).

**Non-biodegradable polymers:** Polyvinyl acetate (PVA), Polydimethylsiloxane (PDS), Polyetherurethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC).

**Mucoadhesive polymers:** Polycarbophil, Sodium carboxy methyl cellulose, Polyacrylic acid, Tragacanth,

Methyl cellulose, Xanthan gum, Guar gum, Karaya gum, Locust bean gum(Aulton M *et al.*, 2007).

## FACTOR AFFECTING RELEASE FROM MATRIX TABLET:

**Physicochemical Factors:**

**Dose size:**

In general, a single dose contains drug about 500mg to 1.0g is considered maximal for a conventional dosage form. Compounds which having large dosing size they given multiple amounts or either formulated into liquid systems. Another consideration is the margin of safety which involves administration of large amount of a drug with a narrow therapeutic range.

**Ionization, pKa and aqueous solubility:**

Most drugs are weak acids or weak bases. While the drugs which are in unchanged form permeate across For drug permeation offering the drug in an unchanged form is beneficial. The aqueous solubility unfortunately will be decreased by conversion to unchanged form, which is more complex. Delivery systems that are dependent on diffusion or dissolution will equally be dependent on the solubility of the drug in aqueous media.

**Stability:**

One important factor for oral dosage forms is the loss of drug through acid hydrolysis or metabolism in the GI tract. Controlled drug delivery systems may provide benefits for highly unstable drugs because the drug may be protected from enzymatic degradation by incorporation into a polymeric matrix (Jantzen G *et al.*, 1995).

## BIOLOGICAL FACTORS AFFECTING RELEASE FROM MATRIX TABLET:

**Biological half-life:**

Drugs which have short half-life are best candidate for Sustain release formulation. Drugs which having shorter half-life less than 2 hours such as levodopa are poor candidates for sustained release Formulation. Drugs which having longer half-life more than 8 hours are also poor candidate for sustained release formulation because their effect is already sustained for examples Digoxin and Phenytoin.

**Absorption:**

The aim of forming the sustained release product is to control the release rate of drug which much slower than the rate of absorption. If we assume that the transit time of most drugs in the absorptive areas of the GI tract is about 8-12 hours, the extreme half-life for absorption should be in the region of 3-4 hours then, the dosage form will pass out of the probable absorptive regions before drug release is complete.

**Distribution:**

The rate of elimination of drugs are primarily depends upon the apparent volume of distribution. So, the drugs with high apparent volume of distribution is influence the rate of elimination of the drug, these drugs are considered to be a poor candidate for oral sustained release drug delivery system for example Chloroquine. (Modi S *et al.*, 2011,
Guptaand R, 2012).

## MOLECULAR SIZE AND DIFFUSIVITY:

Drugs in many sustained - release systems must diffuse through a rate controlling membranes or matrix. The ability of a drug to diffuse through membranes, it is called as diffusivity (diffusion coefficient), is a function of its molecular size (or molecular weight), an important influence upon the value of the diffusivity. 'D', in polymers is the molecular size for molecular weight of the diffusing species.

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