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Review Article

Review on Sustained Release Matrix Tablets

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Abstract

Oral drug delivery is the most preferred option for administration of various drugs. Tablets, Capsules, Syrups, Solutions etc. are administered by this route. Sustain release dosage forms are novel approach in the drug delivery system. Oral sustained release products having promising advantage over conventional drug delivery system. By sustained release delivery system optimization of bio-pharmaceutical, pharmacokinetic and pharmacodynamic characteristics of the drug. Sustain release dosage form also provides the way to decrease the side effects of the drug. There are various advantages of sustained release drug delivery like improved patient compliance, reducing the fluctuation in steady-state drug levels, maximum amount of the drug is used, increased safety margin of potent drugs, reduction in healthcare costs of therapy. Sustained release matrix tablets are widely used. Matrix tablets are prepared by using various types of polymers. This review article focused on the types of polymers used in the preparation of matrix tablets, the methods used to prepare the matrix tablets and all basic information about the sustained release matrix tablets

Keywords: *Sustain release drug delivery, Matrix tablets, Polymers, Evaluation of Matrix tablet*

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Introduction

The advantage of administer a single dose of a drug which released over an extended period of time instead of taking multiple doses of drug is area of interest for scientists in Pharmaceutical industry. Sustained release drug delivery has basic goal to achieve a steady-state blood or tissue level for therapeutically effective and non-toxic for an extended period. There are different types of oral dosage forms that shows modified release properties; includes repeated action, sustained release, extended release and controlled release, delayed release, prolonged release. Modified release dosage forms designed to provide fast achievement of a drug plasma level that remains constant at a value within the therapeutic range for a significant period of time. For the maintaining constant concentration of drug in the body, the two conditions are required that is,

(1)The zero order release of drug,[1]

(2)The rate at which the drug is released from maintenance dose (and subsequently the absorption rate) should be equal to the rate of drug elimination at the required steady-state concentration a list of important terms that describe different modified release dosage forms are defined.[1]

If the active compound has a long half-life, it shows sustained property on its own, If the pharmacological activity is not directly related to its concentration in the blood, absorption of the drug involves an active transport and if active compound has very short half-life, the large amount of drug is required to maintain a prolonged effective dose. The goal of an extended release dosage form is to maintain therapeutic drug level in plasma for extended period of time. Matrix system is widely used for the purpose of sustained release. It is the release system prolongs and controls the release of the drug that is dispersed. Matrix is defined as a well-mixed composite of one or more drugs with gelling agent that is hydrophilic polymers.[2] There are number of polymers used to formulate matrix tablets depending on the physicochemical properties of the drug to be incorporated into matrix system and type of drug release required.[3]

1. Modified release dosage form:
The dosage forms whose drug release characteristics of time period and location are chosen to achieve therapeutic and convenience objectives not offered by conventional dosage forms.

2. Controlled release dosage form:
The drug is released at a constant rate and the drug concentration obtained after administration is invariant with time.

3. Delayed release dosage form:
The drug is released at time other than immediately after administration.

4. Extended release dosage form:
Slow release of the drug so that plasma concentrations are maintained at a therapeutic level for a extended period of time usually between 8 and 12 hours.

5. Prolonged release dosage form:
The drug is used for absorption over a longer period of time than from a conventional dosage form. On the other hand, there is an implication that onset is delayed because of an overall slower release rate from the dosage form.

6. Repeat action dosage form:
The dosage form which indicates an individual dose is released almost immediately after administration, and second or third doses are subsequently released at irregular intervals.

7. Sustained release dosage form:
The drug is released slowly at a rate governed by the delivery system.

Justification for Developing Sustained Release Drug Delivery System[4] :

1. To extend the time duration of action of the drug.
2. To reduce the fluctuations in plasma level concentration.
3. Increased drug utilization.
4. To reduce the frequency of dosing for the uniform drug delivery.

Advantages Sustained Release Drug Delivery[3] :
1) Maintains therapeutic concentrations for prolonged time periods.
2) Reduce the high blood concentration.
3) Reduction in toxicity level by slowing drug absorption.
4) The local and systemic side effects are minimized.
5) Improvement in treatment efficacy.
6) Better drug utilization.
7) Minimize drug accumulation with chronic dosing.
8) Prepare for release high molecular weight compounds.
9) Usage of less total drug.
10) Improved patient compliance.

Disadvantages of Sustained Release Drug Delivery[3] :
1) The remaining matrix must be removed after the drug has been released.
2) Dependent on GI residence Time.
3) Increased potential for first-pass effect.
4) Delay in onset of drug action.
5) Release rate is affected by food and the rate of transit through the gut.

Classification of Sustained Release Drug Delivery System[5] :

1. Diffusion System
   a) Reservior Devices
   b) Matrix Devices
2. Dissolution System
3. Osmotic Pump
4. Ion exchange System
5. Swelling and Expansion System
6. Floating System
7. Biomucoadhesive System
8. Matrix System

Factors Affecting The Sustained Release Drug Dosage Form :

1) Physicochemical Properties

a) Molecular size and diffusivity
b) Aqueous solubility
c) High solubility
d) High permeability
e) pKa Ionization constant
f) Partition coefficient
g) Stability

2) Biological Factors

a) Absorption
b) Distribution
c) Metabolism
d) Dose dependent bioavailability
e) Elimination half life
f) Drug-protein binding
g) Therapeutic index
h) Duration of action

Sustained Release Matrix Tablets :

The matrix system is most widely used for a drug-controlled release from a pharmaceutical dosage form. This is the least complex approach to manufacture of sustained release dosage form by the direct compression of blends of drug, retardants and additives to form a tablet in which drug is embedded in a matrix core of the retardant. Among the many methods used in controlled release drug from pharmaceutical dosage form, the matrix system is the most frequently used; it is release system for delay and control of the release of the drug that is dispersed or dissolved which is retard disintegration. The three class of retardant materials used to formulate matrix tablets that is as follows,

1. Insoluble, inert
2. Insoluble, erodible
3. Hydrophilic

Matrix consist of drug homogeneously dispersed throughout a polymer matrix. The rate limiting step in controlling release from these formulations is liquid penetrate in the matrix unless channeling agents are included to promote permeation of the polymer matrix by water, which occurs as. The drug in the outside layer exposed to the bathing solution is dissolved first then diffuses out from the matrix. This process occurs with the interface between the bathing solution and the solid drug moving towards the interior, for this to be diffusion controlled, the rate of dissolution of drug particles within the matrix must be rapid than the diffusion rate of dissolved drug leaving the matrix[1]. To control the release of the drugs of different solubility properties, the drug is dispersed in swellable hydrophilic substances, an insoluble matrix of non-swellable hydrophobic or plastic materials[4].

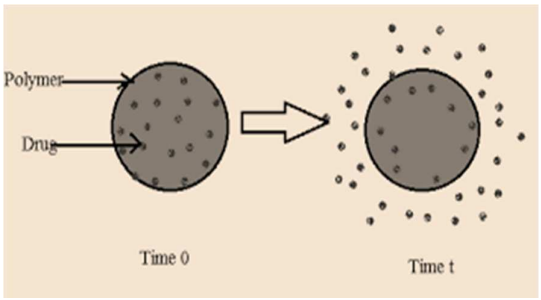


Fig.1: Diagrammatic representation of drug embedded in matrix and release

Types of Matrix[5] :

1. Hydrophobic Matrices :

In this type of matrix used in sustained release from an oral dosage form, drug and an inert or hydrophobic polymer are mixed and then compressed in to a tablet. Sustained release is produced due to the dissolving drug has diffused through channels that exist between compacted polymer particles.

2. Lipid Matrices : These types of matrices prepared by the lipid waxes and related materials. Drug release from this matrices occurs through pore diffusion and erosion. Release characteristics are therefore more sensitive to composition of digestive fluid than to totally insoluble polymer matrix.

3. Hydrophilic Matrices :

Matrix is defined as well mixed composite of one or more drugs with a gelling agent (hydrophilic polymer). These systems also known swellable controlled release systems. There are two types of hydrophilic matrices.

a) Cellulose derivative –
b) Non cellulose natural or semi-synthetic polymers –

4. Biodegradable Matrices :

This type of matrices consist of the polymers consist of monomers linked to one another through functional groups and having backbone of unstable linkage. They are biologically degraded or eroded by enzymes generated by non enzymatic process or living cells in to oligomers and monomers that can be metabolized or excreted.

4. Mineral Matrices :

These type of matrices consist of polymers which are obtained from various species of seaweeds.

On the Basis of Porosity of Matrix[5] :

Three types of matrix system are used.

1. Macro porous systems :
In this systems the diffusion of drug occurs through pores of matrix, which are of size
range 0.1 to 1 µm. This pore size is larger than diffusant molecule size.

2. Micro porous system :
In this type of system diffusion occurs essentially through pores. For micro porous systems, size of pore ranges between 50–200A°, which slightly larger than diffusant molecules size.

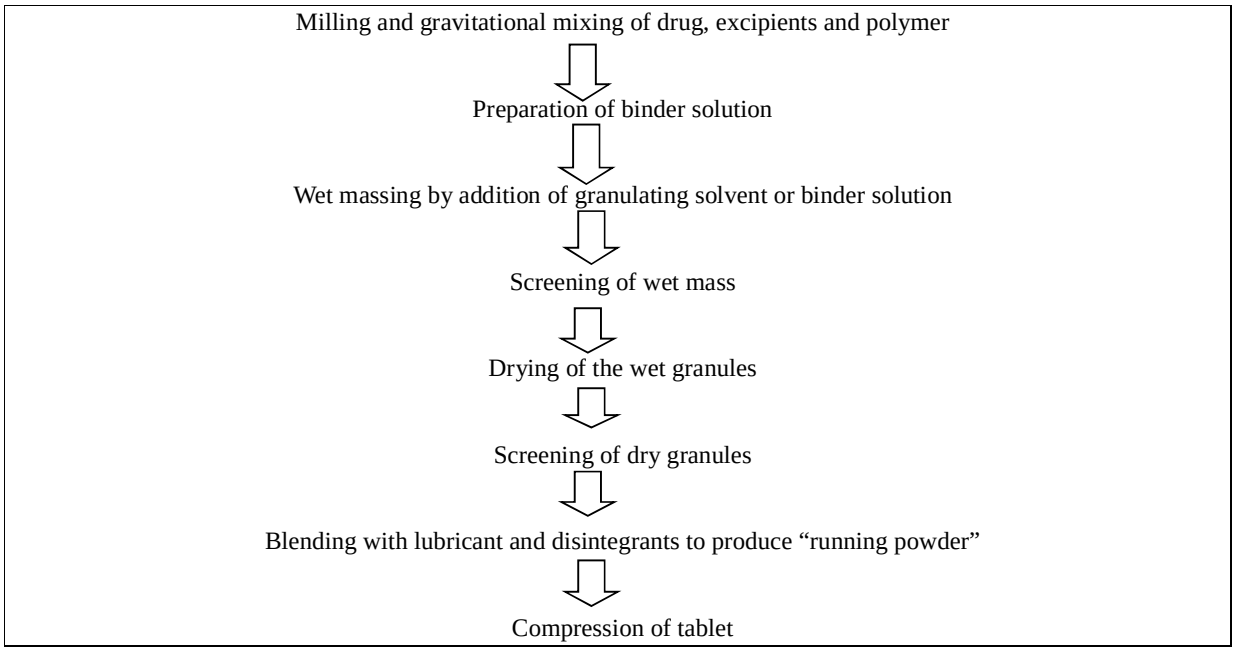
3. Non-porous system :
This type of systems have no pores and the molecules diffuse through the network meshes. In this, only the polymeric phase exists and no pore phase is present.

Table 1 : Types of Matrix Along With Example of Polymers

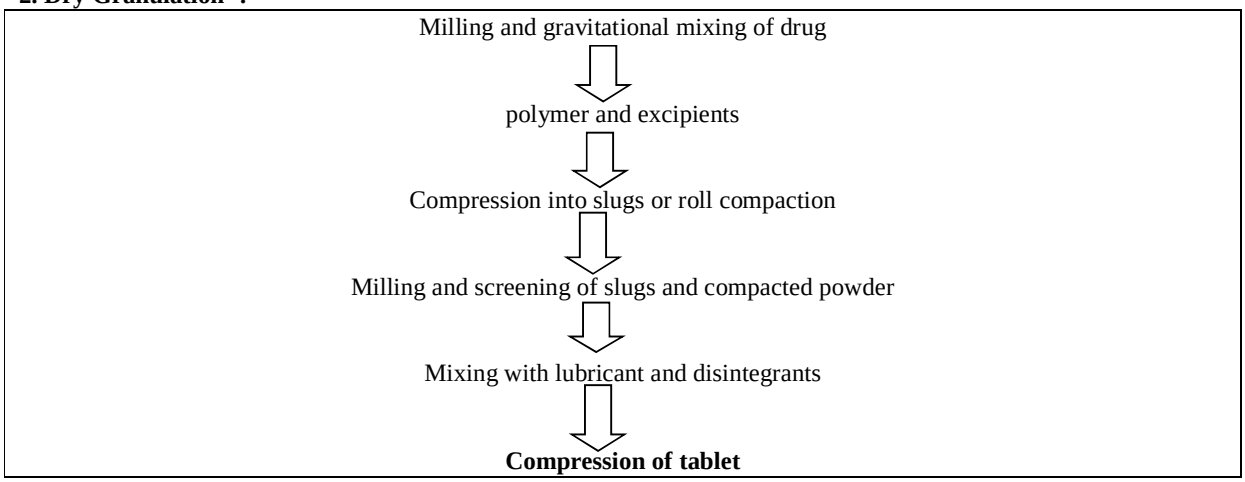
Sr. No.	Types of matrix	Example of polymers
1	Hydrophobic Matrices	polyethylene, polyvinyl chloride, ethyl celluloseand acrylate polymers and their copolymers.
2	Lipid Matrices	Carnauba wax combination with stearyl alcohol or stearic acid
3	Hydrophilic Matrices	Methylcellulose 400 and 4000cPs, Hydroxyethylcellulose, HPMC, Sodium carboxymethylcellulose, Agar-Agar, Carob gum, Alginates, Molasses, Polysaccharides of mannose, galactose, chitosan and modified starches.
4	Biodegradable Matrices	Natural polymers, Proteins, polysaccharides, modified natural polymers, aliphatic poly(esters), poly anhydrides.
5.	Mineral Matrices	Alginic acid hydrophilic carbohydrate obtained from species of brown seaweeds(Phaephyceae)

Methods of Preparation Of Matrix Tablets – Schematic Diagram

1. Wet Granulation[6] :



2. Dry Granulation[6] :



3. Sintering Technique[6] :

Sintering technique is defined as the bonding of adjacent particle surfaces in a mass of powder, or in a compact, by the appliance of heat. Conventional sintering involves the heating of a compact at below the melting point of the solid constituents in a controlled environment under atmospheric pressure. The hardness and disintegration time of tablets changed when stored at
elevated temperatures were described as a result of sintering. This process has been used for the production of sustained release matrix tablets for the stabilization and retardation of the drug release.

3. Melt Granulation[4] :

In this process the substance, which melts at relatively low temperature. This substance added in the molten form over the substrate, which is then heated above its melting point. Different lipophilic binders were tried by using melt granulation technique.

4. Hot-Melt Extrusion Process[4] :

In hot-melt extrusion process, a mixture of the active ingredients, the thermoplastic polymers and other processing aid is fed into the drum of the extruder through the hopper. The materials are transferred inside the heated drum by a rotating screw. The materials melt at elevated temperatures and the molten mass is continuously pumped through the die attached at the end of the drum. Depending upon the dimensions of the die cylinders, films can also be produced from the extruder.

Evaluation of matrix tablets :

1. Weight Variation Test :

The weight of tablet is measured to ensure that a tablet contain the proper amount of drug.

1. The weight variation test is done by weighing 20 tablets individually.
2. Calculate the average weight.
3. Compare the weights of individual tablet to the average weight.
4. The tablets pass the test if not more than 2 tablets go outside the percentage limit.

2. Friability Test :

By this test evaluation of the ability of tablet to abrasion and edge damage during packing, handling and shipping. Friability is measured with the help of Roche friabilator. A number of preweigh tablet is placed in plastic chamber that revolves at 25 rpm for 100 revolutions. Then tablets are de-dusted and reweighed. The friability is calculated by the formula.

$$F = (1- w/w^*) 100$$

Where, W* = the original wt. of tablet
W = the final wt. of tablet after test.
Acceptance limit for friability is 0.5–1%.

3. Hardness Test :

Tablet require a certain amount of hardness to with stand mechanical shock of handling in manufacture , packaging, and shipping. Hardness is measured by using the hanrdness tester like, Monsanto tester
Pfizer tester
Strong cob tester
Hardness measured with the help of Monsanto tester. The tester consist of barrel between two plungers containing a compressed spring. The lower plunger is then forced against a spring by turning a threaded bolt until the tablet fractures. The spring is compressed, a pointer rides along gauge in the barrel to indicate force. The force of fracture is recorded. Hardness measured in kg/cmsq.

4. In Vitro Drug Release :

The In vitro drug release profile of matrix tablet is determine by the USP dissolution apparatus type II. Single matrix tablet is placed in dissolution flask which contain 900 ml dissolution medium. The flask is maintained temperature at 37º±0.5ºC by a constant temperature bath. The motor is adjusted to turn at the specified speed (50rpm) and sample withdrawn at intervals to determine the amount of drug in the solution. Matrix tablet slowly release the drug for prolong period of time.

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