

**Formulation and evolution of matrix tablets- a review**

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**ABSTRACT**

Formulations that are able to control the release of drug have become an integral part of the pharmaceutical industry. Many of the pharmaceutical dosage form are formulated as sustained release dosage form to retard the release of a therapeutic agent such that its appearance in the systemic circulation is prolonged and its plasma profile is sustained in duration. Tablets offer the lowest cost approach to sustained and controlled release dosage forms. Matrix tablets serves as an important tool for oral extended- release dosage forms. Hence, problems like patient compliance, drug targeting, local side effects, frequent administration and fluctuations in blood concentration levels, associated with their counterparts, the conventional dosage forms were solved. Oral extended release drug delivery system becomes a very promising approach for those drugs that are given orally but having the shorter half-life and high dosing frequency. Extended-release drug-delivery system reduces the dosing frequency of certain drugs by releasing the drug slowly over an extended period of time Matrix tablets may be formulated by wet granulation or direct compression methods by dispersing solid particles within a porous matrix formed of hydrophilic and hydrophobic polymers. The use of different classes of polymers in controlling the release of drugs has become the most important aspect in the formulation of matrix tablets.

**Key words:** Matrix tablets, Extended-release**INTRODUCTION:**

Pharmaceutics is the discipline of pharmacy that deals with the process of turning a new chemical entity (NCE) into a medication to be used safely and effectively by patients. It is also called the science of dosage form design. There are many chemicals with pharmacological properties, but need special measures to help them achieve therapeutically relevant amounts at their sites of action. Pharmaceutics helps relate the formulation of drugs to their delivery and disposition in the body. Pharmaceutics deals with the formulation of a pure drug substance into a dosage form. Pure drug substances are usually white crystalline or amorphous powders. Historically before the advent of medicine as a science it was common for pharmacists to dispense drugs as is, most drugs today are administered as parts of a dosage form. The clinical performance of drugs depends on their form of presentation to the patient<sup>(1)</sup>

The oral route of drug delivery is the most popular, desirable and preferred method of administering therapeutic agents for systemic effects because it is natural, convenient for the patient, and cost effective to manufacturing process. One of the most common approaches used for prolonging and controlling the rate

of drug release is to incorporate a drug in hydrophilic colloid matrix such as hydroxypropylcellulose, hydroxypropylmethylcellulose (HPMC), carbopol, methylcellulose, alginates and gelatin. The mechanism and kinetics of release of the drug incorporated in these polymer matrices is dependent on the type and amount of polymer as well as on the physicochemical properties of the drug. Generally drug release from these matrices follow penetration of fluid, followed by dissolution of the drug particles and diffusion through fluid filled pores<sup>(2)</sup>. The diffusion of a drug through a matrix is the rate-limiting step.

In hydrophilic polymer matrix system, zero-order release kinetics can be maintained if the polymer swells at a constant rate, maintaining a constant surface area and the diffusion of the drug is comparatively rapid<sup>(3)</sup>. In addition to matrix system, reservoir or membrane-controlled and osmotic controlled release systems have also been used for prolonging and controlling the drug release rate<sup>(4)</sup>. However, the variable absorbing surfaces over the length of the GI tract adds constraint to the design of oral dosage forms. Moreover, the stomach emptying period varies from person to person. These factors collectively introduce considerable variability in the performance of oral controlled delivery systems<sup>(5)</sup>.

#### ADVANTAGES OFFERED BY MATRIX TABLETS

- Maintains therapeutic concentrations over prolonged periods.
- Avoids the high blood concentration.
- Reduction in toxicity by slowing drug absorption.
- Minimize the local and systemic side effects.
- Improvement in treatment efficacy.
- Better drug utilization.
- Minimize drug accumulation with chronic dosing.
- Can be made to release high molecular weight compounds.
- Increase the stability by protecting the drug from hydrolysis or other derivative changes in GIT.
- Reduction in health care cost.
- Usage of less total drug.
- Improved patient compliance.<sup>(6-7)</sup>

#### DISADVANTAGES OF MATRIX TABLETS

- The remaining matrix must be removed after the drug has been released.
- Greater dependence on GI residence time of dosage form.
- Increased potential for first-pass metabolism.
- Delay in onset of drug action.
- Release rates are affected by food and the rate transit through the gut.
- Release rate continuously diminishes due to increased diffusional resistance and decrease in effective area at the diffusion front.<sup>(6-7)</sup>

#### VARIOUS APPROACHES TO ACHIEVE CONTROLLED RELEASE

##### DRUG DELIVERY

Various techniques have been used in the formulation of controlled release products. In general, controlled release formulations can be divided into different categories based on the mechanism of drug release.

##### ION EXCHANGE RESINS

Ion exchange resins are cross-linked water-insoluble polymers carrying ionizable functional groups. The resins have been used in various pharmaceutical applications, primarily for taste masking and controlled release systems. In tablet formulations, ion exchange resins have been used as disintegrants because of their swelling ability. It forms irreversible complex with ionizable drugs upon prolonged exposure of the drug to the resin. A resin bound-drug is removed when appropriate ions are in contact with ion-exchanged groups. The area and length of diffusion pathway, and the amount of cross-linked polymer in the resin moiety governs the rate of drug release.

##### DISSOLUTION CONTROLLED RELEASE

This type of controlled release involves two processes, the detachment of drug molecules from the surface of their solid structure to the adjacent liquid interface, followed by their diffusion from the interface into the bulk liquid medium. The rate of dissolution and the amount dissolved per unit of time from this system can be calculated using Noyes-Whitney equation (1897). They found that a combination of acrylic acid polymer (mainly Eudragit) with PEO could sustain the release of metformin when administered orally.

##### DIFFUSION CONTROLLED RELEASE

In this type of controlled release system, the active ingredient diffuses through the polymeric material. There are mainly reservoir and matrix systems.

##### (a) RESERVOIR SYSTEM

It consists of a core (the reservoir) and coating membrane (the diffusion barrier). The active ingredient diffuses from the reservoir through the coating membrane. For a reservoir system where the drug depot is surrounded by a polymeric hydrogel membrane, Fick's first law of diffusion can be used to describe drug release through the membrane.

##### (b) MATRIX SYSTEM

A matrix system consists of active and inactive ingredients, that are homogeneously dispersed and mixed in the dosage form. It is by far the most commonly used oral controlled release technology and the popularity of the matrix systems can be attributed to several factors which will be discussed in the later section. The release from matrix type formulations governed by Fick's first law of diffusion.

J is flux, or rate of diffusion, while Q is the amount diffused per unit of time t, and D is diffusion coefficient.

$$J = \frac{dQ}{dt}$$

##### PREFORMULATION STUDIES

- Drug
  - Identification
  - Melting Point
  - Solubility
  - Shape and surface characterization
- Organoleptic properties
- UV characterization
- Bulk density
- DSC (Differential Scanning Colorimetry)
- Angle of repose
- Particle size distribution
- Tapped density

##### EVALUATION PARAMETER:

Prepared tablets were evaluated for certain physical properties like uniformity of weight, hardness, friability and dissolution study etc.

#### UNIFORMITY OF WEIGHT

Every individual tablet in a batch should be in uniform weight and weight variation in within permissible limits. The weights were determined to within  $\pm 1$ mg by using Sartorius balance (BT 124 S). Weight control is based on a sample of 20 tablets.

#### DIMENSIONS

The dimensions (diameter and thickness) were then determined to within  $\pm 0.01$  mm by using digital vernier calipers<sup>14</sup>.

#### HARDNESS

The hardness of the tablets was determined by diametric compression using a Hardness 33 testing apparatus (Monsanto Type). A tablet hardness of about 4-5 kg is considered adequate for mechanical stability.

#### FRIABILITY

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W<sub>0</sub>) or a sample of 400 tablets are dedusted in a drum for a fixed time (4000 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %.

#### IN-VITRO DISSOLUTION STUDY

The release rate of THP SR matrix tablet was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer (pH=6.8), at 37  $\pm$  0.5°C and 100 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 4, and 8 hour. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a 0.45  $\mu$ m membrane filter. Absorbance of these solutions was measured at 271 nm using a UV – 1800; M/s Shimadzu UV/V is double beam spectrophotometer.

#### ACCELERATED STABILITY STUDIES

Optimized formulation were packed in blister and stored in ICH certified stability chambers maintained at 40°C and 75% RH for three months. The tablets were withdrawn periodically and evaluated for drug content and release studies.

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