International Journal for Pharmaceutical Research Scholars (IJPRS)

V-4, I-2, 2015 ISSN No: 2277 - 7873

REVIEW ARTICLE

Disintegration Controlled Matrix Tablet: A Review

Deokate UA*, Wavhale JL

Department of Pharmaceutics, Government College of Pharmacy, Aurangabad, Maharashtra. India- 431005.

Manuscript No: IJPRS/V4/I2/00111, Received On: 28/05/2015, Accepted On: 07/06/2015

ABSTRACT

A number of technologies are available to control or modify the drug release from a dosage form. Mostly are of oral dosage form and they are categorized as matrix, reservoir or osmotic system. This review focused on the Disintegration Controlled Matrix tablet (DCMT) formulation development. The solid dispersion containing water soluble matrix forming agent, disintegrating agent, and wax mainly produce the DCMT system. With the help of the DCMT drug release can be sustained up-to 24Hrs. This dosage form gives the increase in the solubility and bioavailability of the drug. For drugs having low solubility DCMT is the novel approach for sustain release formulation.

KEYWORDS

Disintegration Controlled Matrix Tablet (DCMT), Solid Dispersion, Wax, Disintegrating Agent, Matrix Forming Agent

INTRODUCTION

Traditional and conventional drug delivery system offers immediate release and repeated dosing of the formulation which result into dose fluctuation and non-patient compliance. To overcome the previous drawbacks the sustain release or controlled release drug delivery system is developed which maintains a constant or uniform blood level.[1] On the basis of release the drug delivery system is divided into different categories as follows

Modified Drug Delivery Systems

Modified dosage forms designed to release the drug over a given period of time or after the drug formulation reaches to the site of action.

Classification: Modified Release dosage forms are classified as follows-

***Address for Correspondence:**
Dr. Uday A. Deokate
Assistant Professor, Department of Pharmaceutical Chemistry,
Hotel Vedanta Road, Osmanpura,
Aurangabad, Maharashtra. (India) 431005.
E-Mail Id: jswavhale1220@gmail.com

1. Extended Release
2. Sustained Release
3. Controlled Release
4. Delayed Release
5. Site-specific targeting
6. Receptor targeting

Extended Release

Oral DDS released the drug over prolonged period of time. By extending the release profile of a drug, the frequency of dosing can be reduced. Extended release preparation can be formulated by using sustained or controlled-release formulation approach. For release the drug at predetermined rate in order to maintain a constant drug concentration for a specific period of time with minimum side effects sustain release drug delivery is used. The onset of action is delayed and therapeutic effect is sustained. Sustained release systems generally imitate zero order release by providing drug in a first order manner. Controlled release dosage form is

© Copyright reserved by IJPRS

referring to the delivery of formulation in response to stimuli or time, generally achieved by obtaining "Zero Order" release from the dosage form which is not drug concentration dependent.

Delayed Release

Delayed-release systems are those that use repetitive, intermittent dosing of a drug, from one or more immediate-release units incorporated into a single dosage form. Examples repeat-action tablets and capsules, enteric coated tablets where time release is achieved by a barrier coating.

Site-specific Targeting

Site-specific drug delivery refers to delivery of a drug directly to a certain biological location. In case of site-specific release, the target is situated nearby or on the diseased organ or tissues.

Receptor Targeting

For receptor release, the particular receptor is targeted for a drug within an organ or tissue. Both of these systems satisfy the special aspect of drug delivery and are also considered to be controlled drug-delivery system.

Sustained Release Drug Delivery Systems

During the past few years, conventional dosage forms of drugs are rapidly being replaced by the new drug delivery systems, amongst these the controlled / sustained release dosage forms admired by physician as well patient. The basic rationale for sustained release drug delivery is to modify the pharmacokinetics and pharmacodynamics of drugs by using novel drug delivery systems or by modifying the molecular structure or physiological parameters inherent in a selected route of administration. It is desirable that the duration of drug action becomes more a design property of a rate controlled dosage form and less or not at all a property of the drug molecule's inherent kinetic properties. Thus, optimal design of a sustained/ controlled release system necessitates a thorough understanding of the pharmacokinetics and pharmacodynamics of the drugs.

Sustained release drug administration means not only the prolongation of duration of drug delivery similarly to the action in the sustained and prolonged release, but the term also implies the predictability and reproducibility of drug release kinetics. The controlled release of drug substances and their effective transport to sites of action can be exploited to maximize the beneficial clinical response and to minimize the incidence of unbeneficial adverse reactions and side effects.

Several approaches is used to formulate the controlled or sustained release drug delivery systems including matrix system, osmotic drug delivery system, coated tablets, reservoir drug delivery system, etc. Beside this some novel delivery system approaches were made like palletisation, hot melt extrusion. Among this the disintegration controlled matrix tablet (DCMT) is one of the novel approach is used to formulate sustained release DDS. The current review presents the significance of the DCMT, its formulation, and other relevant information regarding the DCMT.

Disintegration Controlled Matrix Tablet (DCMT)

DCMT is the novel approach employed for sustaining the drug release. The drug release is controlled by the penetration of water in the matrix which is rate determining step for dissolution of the DCMT. DCMT contains water soluble matrix forming polymer, disintegrating agent, and wax. In this preparation rate of the release decreases due to the decrease in the concentration gradient and the increase in the distance of diffusion, and therefore the amount of the release is approximately proportional to the square root of the time.[2]

These system release the drug from the matrix by different types of the mechanism such as follows

1. Diffusion controlled
2. Dissolution controlled
3. Surface erosion

© Copyright reserved by IJPRS

Theory of DCMT for Drug Release

In disintegration controlled matrix tablet follows the surface erosion phenomenon for the drug release. The drug is distributed uniformly throughout the polymer matrix and the diffusion rate of the drug in the matrix is very slow compared to polymer dissolution. The difference between erodible systems and non-erodible systems is that the polymer phase in non-erodible system remains unchanged with time and drug is released by diffusion, while the polymer phase in erodible system decreases with time.[3]

Hoffenberg propose the general mathematical equation for describing the drug release from the surface erodible systems such as sphere, tablet, and slabs etc. the equation is follows

$$Mt/M\infty = 1 - \left[1 - \frac{K_0 t}{C_0 a_0}\right]^n \quad \text{.....(1)}$$

In pharmaceutical formulation, from which a drug is released continuously, so that the effect of the drug can be maintained over a long period of time which have so far been studied for the purpose of reducing the dose frequency to be taken by patients and maintaining the blood concentration of a drug below a toxic level, in case that the toxicity or adverse effects of the drug may increase above toxic level. Pharmaceutical preparation comprising drug-containing granules provided with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed in matrix tablet.

The purpose of the disintegration controlled matrix tablet is to solve the problems like the pH dependency, and mainly to avoid the drawback of the diffusion controlled system as the time laps increases the rate of drug release slows down, etc. the pharmaceutical preparation, wherein the release rate of the drug is nearly constant (zero order release) and the change of the release rate of the drug by the change of the stirring intensity or the pH value is little.

This technique comprises coating the instantaneously disintegrable granules containing drug, with the coating layer consisting of wax, water soluble polymer and nonionic surfactant having HLB not more than 9 and after that, compressing the resultant coated granules into tablets to give sustained release tablets.

In this method there are many factors which affect on the drug release such as the combination ratio of the wax: disintegrating agent. The disintegration controlled matrix tablet contains the drug, disintegrating agent, wax and water soluble matrix forming polymer.

The rate-determining step of the drug release from the tablet of the formulation, where the inner granules in the surface layer of the tablet disintegrate (or separate) from the tablet, and this characteristic gives rise to the feature of the tablet of the present invention that the dissolution pattern is linear and that the dissolution pattern and the dissolution rate are hardly influenced by the change of the intensity of stirring or the pH of the aqueous medium.

Parenthetically, as mentioned before, sustained release tablets of the present invention may contain water soluble polymer, namely, may comprise easily disintegrable granules containing drug together with water soluble polymer, and wax. In this case, the duration of the drug release or the like can be controlled more precisely by further adjusting the molecular weight of the water soluble polymer to be used. The higher the viscosity of the water soluble polymer (namely, the molecular weight of the water soluble polymer) became, the longer the duration of the dissolution became. As stated above, it is possible to adjust the properties of the tablets of the present invention such as the duration of the dissolution or the dissolution rate by adjusting the molecular weight of the water soluble polymer to be used without losing the features such as almost constant dissolution rate, and the independency of dissolution pattern on the pH of the dissolution medium.

Therefore, it is possible to adjust the properties of the tablets more specifically by the combination of adjusting the kind and/or the amount of the disintegrating agent, adjusting the kind and/or the amount of the wax and adjusting the molecular weight of the water soluble polymer.

© Copyright reserved by IJPRS

The diagrammatic representation of mechanism of the drug release through the disintegration controlled matrix tablet is as follows

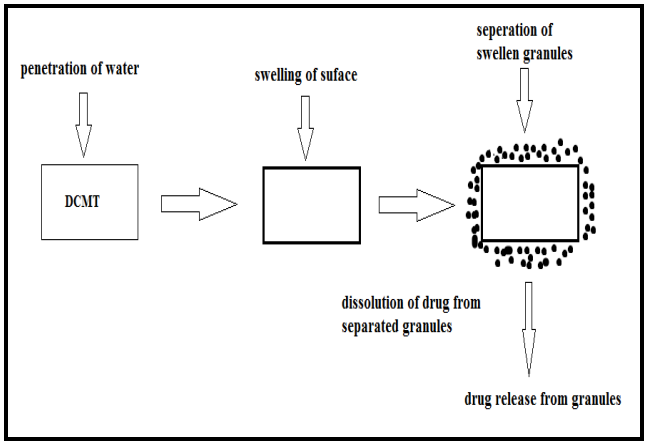

Figure 1. Mechanism of drug release from DCMT

Advantages of the Disintegration Controlled Matrix Tablet (DCMT)[4]

1. Drug release is pH independent
2. Drug release is controlled by the dissolution as well as the diffusion or may be disintegration phenomenon
3. Constant (zero order kinetics) drug release achieved
4. DCMT sustain the drug without re-crystallization.
5. DCMT successfully achieve the complete dissolution and absorption of the drug.
6. Drug absorbed by maintaining the function of the gastric transit.

Method of Preparation of the Disintegration Controlled Matrix Tablet

There are various methods for the preparation of the disintegration controlled matrix tablet as this technique is useful for the poorly water soluble drug candidate so it may include the methods by which the solubility of the drug may improve such as

Solid Dispersion

SD concept is introduced by Sekiguchi and Obi (1961).[5] The term "Solid Dispersion" refers to the dispersion of one or more active ingredients in an inert carrier in a solid state, commonly prepared by the melting (fusion) method, solvent method or melt-solvent method. However, the definition can now be broadened to include certain nanoparticles, microcapsules, microspheres and other dispersion of the drug in polymers prepared by using any one of the process. Sekiguchi and Obi suggested that the drug was present in a eutectic mixture in a microcrystalline state. All drugs in SD are not necessarily present in a microcrystalline state, a certain fraction or part of the drug might be disperse in the matrix.[6] Once the SD was exposed to aqueous media the carrier gets dissolved and the drug was released as very fine colloidal particles. Due to the enhanced surface area obtained it is expected that the dissolution rate and the bioavailability of poorly water-soluble drugs were enhanced. The commercial use of such systems has been limited primarily because of manufacturing problems with SDs which can be overcome by using surface active and self-emulsifying carriers.

Uses of the Solid Dispersion

1. To obtain a homogeneous distribution of a small amount of drug in solid state.
2. To stabilize the unstable drug.
3. To formulate sustained release regimen of soluble drugs by using poorly water soluble or insoluble carriers.
4. To convert polymorphs into isomorphs, solid solution, eutectic mixture or molecular adducts.

Method of Preparation of the Solid Dispersion

- Melt/Cool method
  - Melting solvent method
  - Hot stage extrusion
- Solvent evaporation
  - Hot plate drying
  - Vacuum drying
  - Slow evaporation at low temperature
  - Rotary evaporation

© Copyright reserved by IJPRS

- Spray drying
- Freeze drying
- Spin drying
- Fluid bed coating

- Co-precipitation
  - Addition of an anti-solvent

Formulation Development of DCMT

For the preparation of the DCMT formulation consideration are as follow-

1. Suitable drug candidate
2. Matrix forming agent
3. Disintegrating agent
4. Wax

Drug Candidate

For the preparation of DCMT all drug candidate are suitable but the poorly water soluble drug candidates are mostly preferred. The drugs belongs to the BCS class I and BCS class III are highly soluble and may be sustain by formulating into the DCMT. For example Nilvadipine, Eletriptan Hydrobromide, Sumatriptan Succinate, etc.

Matrix Forming Agent

In the preparation of the DCMT matrix forming agent play an vital role in controlling the drug release, the release is mostly depend on the polymer which is used in the formulation which are generally synthetic or semi-synthetic in nature. Synthetic polymers are used for the preparation of the DCMT the polymers like poly (hydroxyalky1 methacrylate), poly (viny1 alcohol) and their copolymers, poly (ethy1ene oxide) are used. Semi-synthetic polymers are cellulose ethers such as hydroxypropyl cellulose (HPC), methylcellulose (MC), hydroxypropyl methylcellulose (HPMC) and sodium carboxy methylcellulose (Na CMC). Depending on the polymer used, drug release from the tablets may be swelling-controlled, disintegration-controlled, multiple mechanism controlled.

Though the release from the matrix is depend upon the other factors such as the pore permeability, shape and size of matrix, high solubility, polymer molecular weight, drug solubility, drug loading, compression force and hydrodynamic conditions.[7]

The use of the matrix forming agent in the preparation of the DCMT 2.5 to 45 weight percent (more preferably 5 to 30 weight percent) of the whole granule components.[2]

Disintegrating Agent

The disintegration controlled matrix tablet can be prepared by using the various disintegrating agents like, disintegrating agent [e.g. various starch derivatives (e.g. corn starch, potato starch, rice starch, α-starch and carboxymethyl starch), gums (e.g. gum arabic), cellulose derivatives (e.g. calcium carboxymethylcellulose, sodium carboxymethylcellulose, low substituted hydroxypropylcellulose and cross-linked sodium carboxymethylcellulose), various ion-exchange resins (e.g. potassium polymethacrylate], excipient (e.g. lactose, sucrose and mannitol) and commonly used additives in this field of the art, into granules according to a conventional manner.

The amount of the disintegrating agent is preferably 10 to 60 weight percent of the whole granule components.[2]

Wax

The wax to be used in this step includes all kinds of wax insoluble or hardly soluble in water, and may include plant or animal wax (e.g. carnauba wax and bees wax), various hydrogenated oils (e.g. hydrogenated soybean oil, and hydrogenated castor oil) paraffin (e.g. paraffin wax and microcrystalline wax). The wax as mentioned above may be used as a coating of the granules. The wax plays a vital role in the penetration of the water, due to this action the disintegration rate can be controlled and drug release is also controlled. The amount of the wax to be used is fittingly determined depending on the property of the drug to be used, the intended duration of the drug release. The preferable amount of the wax is 20 to 65 weight percent, most preferably 30 to 55 weight percent of the whole components of the tablet, most preferably

© Copyright reserved by IJPRS

30 to 55 weight percent of the whole components of the tablet. Wax is generally used for the coating of the granules which are prepared. The coating layer or matrix comprises a substance insoluble or hardly soluble in aqueous body fluids and the release of the drug is controlled by avoiding the water penetration in the matrix. These pharmaceutical formulation are characterized in that the granules to be coated with the wax which is to be used in making matrix tablets are as hardly disintegrable as possible. The release of the drug from such pharmaceutical formulation provided by the gradient of the drug concentration resulting from penetration of water (diffusion rate-determining).

CONCLUSION

DCMT is sustained release tablet dosage form that increases solubility as well as stability of drug. It maintains the GI transit in case of geriatrics patients without altering its release pattern. DCMT gives the diffusion control release (zero order kinetics), as it prevents penetration of the water in matrix. Due to this action the complete dissolution and absorption of the drug through G.I.T. DCMT is novel approach for the drugs having low solubility and bioavailability in treatment of prolong therapy.

REFERENCES

1. Ankit, B., Rathore, R. P. S., Tanwar, Y. S., Gupta, S., & Bhaduka, G. (2013). Oral sustained release dosage form: an opportunity to prolong the release of drug. *International Journal of Advanced Research in Pharmaceutical and Bio sciences*, *3*(1), 7-14.
2. Sustained release tablet EP 0168044 B1.
3. Katzhendler, I., Hoffman, A., Goldberger, A., & Friedman, M. (1997). Modeling of drug release from erodible tablets. *Journal of Pharmaceutical Sciences*, *86*(1), 110-115.
4. Tanaka, N., Imai, K., Okimoto, K., Ueda, S., Tokunaga, Y., Ohike, A., & Kimura, T. (2005). Development of novel sustained-release system, disintegration-controlled matrix tablet (DCMT) with solid dispersion granules of nilvadipine. *Journal of Controlled Release*, *108*(2), 386-395.
5. Sekigushi, K. and Obi, N. (1961). Studies on Absorption of Eutectic Mixture. I. A Comparison of the Behavior of Eutectic Mixture of Sulfathiazole and that of Ordinary Sulfathiazole in Man. *Chemical and Pharmaceutical Bulletin*, *9*(11), 866-872.
6. Goldberg, A. H. (1966). Increasing dissolution rates and GIT absorption of drugs via solid solutions and eutectic mixture II-experimental evaluation of a eutectic mixture; urea-acetaminophen system. *Journal of Pharmaceutical Sciences*, 55, 482-487.
7. Veiga, F., Salsa, T., & Pina, M. E. (1998). Oral controlled release dosage forms. II. Glassy polymers in hydrophilic matrices. *Drug Development and Industrial Pharmacy*, *24*(1), 1-9.
8. Kim, H., & Fassihi, R. (1997). Application of binary polymer system in drug release rate modulation. 2. Influence of formulation variables and hydrodynamic conditions on release kinetics. *Journal of Pharmaceutical Sciences*, *86*(3), 323-328.

© Copyright reserved by IJPRS