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A REVIEW ON DISINTEGRATION CONTROL MATRIX TABLETS

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ABSTRACT

A number of sustained release formulations are available in the market which successfully sustained the drug release over a prolonged period of time by different mechanisms. The new approach for sustaining the drug release is disintegration control matrix tablet which sustained the drug release up to 24hrs by controlling the disintegration rate of tablet. Disintegration control matrix tablet (DCMT) mainly forms the granules containing drug and disintegrating agent such as low substituted hydroxyl propyl cellulose by various methods such as solid dispersion technique. The sustained release of drug is maintained by increasing the wax coating or decreasing the amount of disintegrants. The release of drug from tablet is uniform throughout till all the drug releases from tablet as it involves drug release by diffusion, dissolution and surface erosion mechanism. DCMT increases the solubility of drug and improves the bioavailability without disturbing gastrointestinal transit. BCS Class II, III, IV drugs are the best candidate for DCMT formulations.

Keywords: Disintegration control matrix tablet (DCMT), Wax, Disintegrating agent, Solid dispersion.

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INTRODUCTION

Disintegration control matrix tablet (DCMT):

DCMT is the novel approach employed for sustaining the drug release and increasing the solubility and bioavailability of drug. The drug release is controlled by the penetration of water in the matrix which is the rate determining step for dissolution of the DCMT. It contains water soluble matrix forming polymer, disintegrating agent, and wax which is insoluble or hardly soluble in aqueous body fluids and the release of drug is controlled by means of said resistance of coating layer or matrix against the diffusion of drug therein. In this preparation, the 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. [1, 2]

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1. Diffusion controlled: DCMT mainly contains disintegrating agent in various concentrations along with matrix forming polymer which are coated by wax and makes the drug release diffusion control, the coating material used is insoluble or hardly soluble in aqueous body fluids which resist the penetration of water in the tablet and due to the presence of water soluble polymer and disintegrants on the surface of tablet gets swells and diffuses the

granules from the swollen surface after they are being dissolved.

2. Surface erosion phenomenon: This is the main mechanism by which the drug is released in DCMT, the presence of wax and water soluble polymer makes tablet to swells, due to swelling the water penetrates the swelling surface causes dissolution of drug and diffusion out of the swollen matrix. The drug release rate is highly dependent upon polymer swelling rate and the drug solubility. This system minimizes the risk of burst release of drug and prevents the dose dumping of drug.
3. Dissolution controlled: The DCMT being the dissolution control however the dissolution is controlled to extend by the use of sustaining polymer such as HPMC. This polymer retard the drug dissolution in the formulation which delays its release time in the formulation, however the dissolution and the diffusion process occur simultaneously during the drug release in the DCMT.[3]

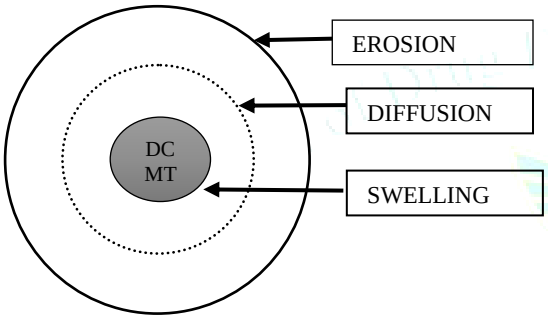

Figure 1: Diffusion controlled drug delivery [4]

Drug release in DCMT:

DCMT follows the surface erosion phenomenon for drug release. The drug is distributed uniformly throughout the polymer matrix and the polymer phase in the erodible system decreases with time. However, in non-erodible system, the polymer phase remains unchanged with time and the drug is released by diffusion phenomenon.

The drug release from surface erodible systems such as tablet, sphere, slabs and so on has been described in the form of mathematical equation proposed by Hoffenberg as follows:

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

DCMT comprises of the granules containing drug and disintegrating agent which is formed by solid dispersion technique ,with the coating layer consisting of wax or hydrogenated soya bean oils, water soluble polymer and non-ionic surfactants(HLB <9) which is finally compressed into tablet to give sustain release formulation. The ratio of disintegrants: wax is very important to produce DCMT. The dissolution rate can be adjusted by using various grades of water soluble polymer in which increase in molecular weight increases the viscosity of the polymer which helps dissolution to became longer without altering other features. The main purpose of DCMT is to avoid drawbacks of diffusion control matrix tablet, reduce the dosing frequency, avoid the pH dependency for drug release, constant rate of drug release i.e. zero order release. [5]

Mechanism of drug release in DCMT:

The drug release from DCMT starts with the penetration of water which leads to the swelling of the tablet surface due to the presence of insoluble polymer and soluble polymer. The swollen granules starts to separate from the tablet surface by diffusion and surface erosion phenomenon and finally the dissolution of drug from the separated granules the mechanism of drug release is described in the following figure [6]

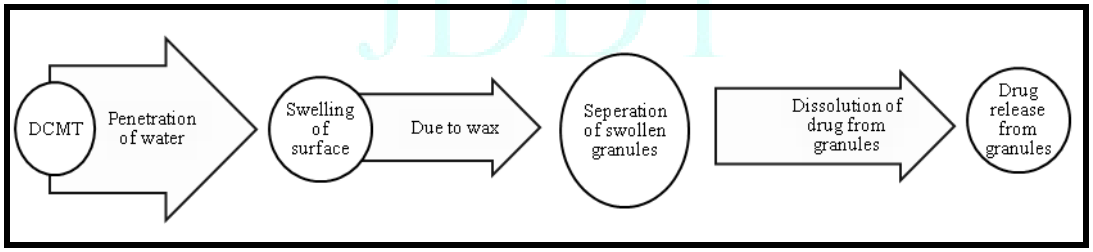

Figure 2: Mechanism of drug release from DCMT[2]

Ideal drug candidate for DCMT:

The drugs that are poorly water soluble usually BCS class II and the drugs which readily recrystallize after the drug release, as happens in most of the cases of solid dispersion granules, are the ideal drug candidates for DCMT. In addition other class of drugs such as BCS class III&IV are also good drug candidate for the sustain release formulation as this sustains the drug successfully up to 24hrs.The drugs having the stability problem such as photo-stability are also considered ideal drug candidate for the disintegration control matrix tablet. [6]

Criteria for sustain release formulations:

To develop a sustain release formulation, the drug must have half-life less than 7hrs and the dose of the drug should not be too large as it will create the problem in sustaining the drug release and also the dose dumping may occur due to large dose size. The drug must be stable in the intestine as sustain release formulation because it has to remain for longer duration of time and release the drug. The drug should have high therapeutic index and the molecular weight should be less than 1000 Daltons. [7, 8]

Principle of sustained release drug delivery system:

In sustained release formulation the rate of drug release is very less than the rate of absorption and the rate of drug release from dosage form is the rate limiting step which make the sustain release formulation to follow zero order kinetics as shown in the following equation,

$$Kr° = Rate\ In = Rate\ Out = Ke\ Cd\ Vd$$

Where, Kr°: Zero-order rate constant for drug release-Amount/time, Ke: First-order rate constant for overall drug elimination-time, Cd: Desired drug level in the body – Amount/volume, and Vd: Volume space in which the drug is distributed in liter. [9, 10]

Advantages of DCMT:

The biggest advantage of DCMT is to increase the solubility of poorly water soluble drugs which is being completely dissolved and absorbed without disturbing the gastrointestinal transit. The drug releases at constant rate by zero order kinetics which is not dependent on the pH and maintains the constant release of drug up to 24hrs without its recrystallization after release. The DCMT provides coating to the drug or granules which will not only mask the bitter or unacceptable taste or odour of drugs but also imparts stability to unstable drugs which might gets affected by the atmospheric condition such as light or moisture. [11]

Disadvantages of DCMT:

DCMT involves three steps in the preparation which is thought to be time consuming, laborious and makes it expensive. The ratio of the wax and disintegrants should be in exact ratio and in proper proportion otherwise the formulation will not might follow the DCMT pattern for the release of drug.

Formulation components of DCMT:

Suitable drug:

The drugs having poor water solubility usually BCS Class-II is usually considered best for the formulation of DCMT. Other class of drugs are also used only to develop a sustain release formulation. Drugs having stability problem (drugs having photo unstability) are also good candidates to develop DCMT.

Disintegrating agent:

The amount of disintegrating agent used in DCMT is about 10-60 % of the whole granule component; however the exact quantity can be determined during the optimization of its formulation. Various types of disintegrating agents are used in the formulation of DCMT such as; starch derivatives (corn starch, potato starch, rice starch, carboxy methyl starch), cellulose derivatives (sodium carboxy methyl cellulose, low substituted hydroxyl methyl cellulose(L-HPC), calcium carboxy methyl cellulose), gums (gum Arabic), ion exchange resins (potassium polymethacrylate).

Matrix forming agent:

The amount of matrix forming agent used in DCMT is usually 5-30 weight percent of whole granule component. This gent plays a vital role in controlling the release of drug from the tablet. The matrix forming agent used may be synthetic of semi synthetic in nature which is selected depending on the type of release required in the formulation. The most common matrix forming agent used in DCMT is hydroxyl propyl methyl cellulose (HPMC) of various viscosity grades most commonly K-100M viscosity grade in sustained release formulations.

Coating agent:

Wax or hydrogenated oils are used as a coating agent for the coating of granules. The amount of wax or hydrogenated oils used in DCMT is preferably 30-65 % by weight of whole granule component. The wax or hydrogenated oils used for coating of granules should be hardly soluble or insoluble in water. The wax plays vital role in the penetration of water which in turn is used to control the disintegration rate and the drug release.

Table 1: Examples of formulation component of DCMT [2,6,12,13]

Formulation Component	Examples
Drug	Fabuxostat
	Eletriptan HBr
	Duloxetine HCl
	Fluvastatin
	Zidovudine
	Ziprasidone HCl
Disintegrating agent	Alginic acid
	Sodium alginate
	Crosspovidone
	Crosscarmillose
	Sodium starch glycolate
	L-hydroxypropyl cellulose(L-HPC)
	Corn starch
	Gum Arabic
	Potassium polymethacrylate
Matrix forming agent	(HPMC-K4M, HPMC-K-100M
	Sodium carboxy methyl cellulose
	Methyl cellulose
	Vinyl alcohol
	Ethylene oxide
	Hydroxyalkyl methacrylate
	Hydroxyl propyl cellulose
Coating agent	Carnauba wax
	Bees wax
	Hydrogenated soyabean oil
	Hydrogenated castor oil
	Paraffin wax
	Microcrystalline wax

Dose calculations in sustain release formulation of DCMT:

D_t= Dose $(1+0.693*t/t_{1/2})$
Where,
D_t= total dose of drug,
Dose= dose of immediate release part,
t= time during which sustained release is desired,
$t_{1/2}$= half life of drug. [14]

Preparation of disintegration control matrix tablet:

Preparation of DCMT consists of three main processes such as preparation of solid dispersion granules, treatment or coating of granules with coating agent and finally compression of granules into tablet.

Importance of solid dispersion:

Solid dispersion (SD) is one of the processes used in the formulation of DCMT to prepare granules. SD is a widely accepted method to increase the solubility, dissolution and bioavailability of poorly water soluble drugs with increased absorption efficiency compared to parent drug. Improved solubility of drugs leads to decrease the dose and the dosing frequency of the formulation and ultimately the side effect, adverse effects and toxic effects. SD plays important role in the uniform distribution of a small amount of drug in solid state there by rendering the chances of dose dumping. The stability of the formulation is widely increased due to solid dispersion technique. [15]

Methods of preparation of solid dispersion:

The solid dispersion is prepared by different methods which are mentioned below but till present literature the SD in disintegration control matrix tablet were prepared by two method i.e. solvent evaporation (vacuum drying) method and the kneading method.

Melt or cool method:

The melt or cool method includes two methods for the preparation of granules as melting solvent method and hot stage extrusion method.

Solvent evaporation method:

This is the another method used in the preparation of solid dispersion and include various methods for preparation of solid dispersion by this method such as vacuum drying, solvent evaporation, slow evaporation at low temperature, hot stage drying, spray drying, freeze drying.

Co-precipitation method:

This is the method of preparation of solid dispersion by precipitation from solution and includes method as Addition of an anti-solvent. [16, 17]

CONCLUSION

Disintegration control matrix tablet is sustained release formulation that releases the drug in zero order kinetics with increase in solubility and bioavailability of poorly water soluble drugs. DCMT achieves the complete absorption of drugs without disturbing the gastrointestinal transit as in case of geriatrics patients. This is completely new approach for poorly water soluble drug as sustain release formulation which sustains the drug up to 24 hrs.

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