INTERNATIONAL JOURNAL OF PHARMACEUTICS & DRUG ANALYSIS
VOL.4 ISSUE 4, 2016; 153 – 159 ; http://ijpda.com; ISSN: 2348-8948

REVIEW ARTICLE

MATRIX TABLET DOSAG-ES FORM AS MOST FAS-CINATING MEMBER OF CONVENTIONAL DRUG DELIVERY SYSTEM-A REVIEW

Harjaskaran*, Kapil Kanwar, Surya Prakash Gautam, Narinder Singh, Lovepreet Singh, Ankit Verma, Amanjot, Shalu Rani.

Department of Pharmaceutics, CT institute of Pharmaceutical Sciences, Shahpur, Jalandhar.

Date Received: 19th March 2016; Date Accepted: 28th March 2016 Date published: 2nd April 2016

email: pharmacist.harjaskaran@gmail.com

Abstract: In the present investigation Matrix tablets serves as a vital instrument for oral controlled dosage forms. Disputes like patient consistence, drug focusing on, neighborhood reactions, successive organization and vacillations in blood fixation levels, connected with their partners, the routine measurements structures were amended. Several of the pharmaceutical dosage form are formulated as controlled release dosage form to delay the release of a therapeutic agent such that its appearance in the systemic course is delayed and its plasma profile is managed in term. Tablets offer the least cost way to deal with controlled sustained release dosage forms. Matrix tablet as controlled discharge has given another leap forward for novel medication conveyance framework in the field of pharmaceutical innovation. This review concentrates on the different sorts of lattice frameworks in light of polymer utilized and porosity of network framework i.e. hydrophilic, hydrophobic, fat wax, permeable, non-permeable, pH sensitive.

Key words: Polymer, Matrix system, Novel Drug delivery system, patents, technique Controlled Release

INTRODUCTION:

Introduction

Oral organization of medications has been most picked course for arrival of chiefly helpful specialists by an assortment of pharmaceutical products of various kind of dose structures. Controlled or Sustained discharge drug conveyance fundamental intention to plotting the rate of discharge additionally keep up yearning drug level in the blood that is non-lethal and restoratively productive for boundless time of time. This likewise gives extended other than not basically steady arrival of the drug. The inspiration for advancement of a controlled discharge definition of a medication is to enhance and Increase its helpful advantages, minimize the side effect[1,2]. CR tablets are readied dynamic constituents are perpetual in a grid of insoluble substance (some chitin, acrylics, regularly licensed). So dissolving drug needs to discover implies out all through the openings in the matrix. Sustained discharge frameworks include one medication conveyance framework which accomplish moderate arrival of medication in surfeit of an amplified timeframe. The onset activity of SR pharmacologic activity is as often as possible delayed. Hydrophilic frameworks are for the most part worn as oral medication conveyance frameworks furthermore more analyze for supported discharge applications because of their great quality among the hydrophilic polymers[3]. the two predominantly critical component of medication conveyance are spatial task and dissident conveyance of a medication. Spatial task describe to the goal a medication to a particular tissue or organ, while consecutive conveyance alludes to controlling the rate of medication conveyance for target tissue. A legitimately thought to be maintained discharge drug-conveyance framework can be a key proceed onward fathoming two problems[4]. The status of oral course is certify to patient compliance, exact dosing, simplicity of organization and practical assembling techniques, likewise conventional conviction that oral Administration the medication is also retained and gastrointestinal physiology propose included versatility in dose structure outline other than the most tablets[5].

Merits and Demerits of Matrix Tablet[6, 7]

Merits:

Benefits of Matrix Tablets are

- Simple to define

- Versatile, productive and shabby.
- High molecular weight compounds can be discharged by framework.
- Retain remedial powerful focuses over delayed periods.
- The utilization of manage discharge details keeps away from the high blood focus.
- Sustain discharge details have the conceivable to enhance the patient consistence.
- Reduce the lethality by abating drug ingestion.
- Prevent drug hydrolysis.
- Reduce the symptoms.
- Enhancement in treatment adequacy.
- Minimize drug collection with endless dosing.
- Usage of less aggregate medication.
- Enhancement the bioavailability of a few medications.

Demerits:

Demerits of Matrix Tablets are:

- The remaining grid must be segregated after the medication has been discharged.
- Greater reliance on GI habitation time of dose structure.
- Increased potential for first-pass digestion system.
- Delay in onset of medication activity.
- Release rates are influenced by nourishment and the rate travel through the gut.
- Release rate consistently reduces because of expanded diffusional resistance and diminishing in successful zone at the dissemination front.

Classification of Matrix System [8, 9]

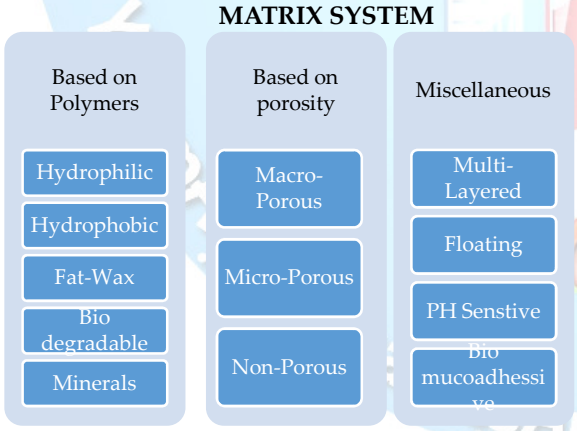

Figure no 1. Classification of matrix tablets

In Briefly Classification of matrix tablets:

Hydrophobic Matrices (Plastic networks):

The idea of utilizing hydrophobic or dormant materials as network materials was initially presented in 1959. In this strategy for acquiring managed discharge from an oral measurements structure, medication is blended with an idle or hydrophobic polymer and after that packed into a tablet. Maintained discharge is delivered because of the way that the dissolving drug has diffused through a system of channels that exist between compacted polymer particles. Cases of materials that have been utilized as inactive or hydrophobic networks incorporate polyethylene, polyvinyl chloride, ethyl cellulose and acrylate polymers and their copolymers. The rate-controlling stride in these plans is fluid infiltration into the framework. The conceivable component of arrival of medication in such sort of tablets is dispersion. Such sorts of lattice tablets get to be dormant in the vicinity of water and gastrointestinal fluid[10].

Lipid Matrices: These networks arranged by the lipid waxes and related materials. Drug discharge from such frameworks happens through both pore dissemination and disintegration. Discharge attributes are in this manner touchier to digestive liquid structure than to absolutely insoluble polymer lattice. Carnauba wax in blend with stearyl liquor or stearic corrosive has been used for retardant base for some supported discharge formulation[11].

Hydrophilic Matrices: Hydrophilic polymer framework frameworks are generally utilized as a part of oral controlled medication conveyance due to their adaptability to acquire an attractive medication discharge profile, cost viability, and expansive administrative acknowledgment. The detailing of the medications in thick containers or all the more as often as possible, in tablets, utilizing hydrophilic polymers with high gelling limits as base excipients is specifically compelling in the field of controlled discharge. Taint a network is characterized too blended composite of one or more medications with a gelling operator (hydrophilic polymer). These frameworks are called swellable controlled discharge systems[12]. The polymers utilized as a part of the planning of hydrophilic networks are isolated into three general gatherings:

A. Cellulose Derivative: Methylcellulose 400 and 4000cPs, hydroxy ethyl cellulose; hydroxy propyl methylcellulose (HPMC) 25, 100, 4000 and 15000cPs; and Sodium carboxy methylcellulose.

B. Non cellulose normal or semi synthetic polymers: Agar-Agar; Carob gum; Alginates; Molasses; Polysaccharides of mannose and galactose, Chitosan and Modified starches. Polymers of acrylic corrosive: Carbopol-934, the most utilized assortment.

Biodegradable Matrices: These comprise of the polymers which included monomers connected to each other through utilitarian gatherings and have flimsy linkage in the spine. They are naturally debased or disintegrated by catalysts produced by encompassing living cells or by

nonenzymetic process into oligomers and monomers that can be metabolized or discharged. Cases are common polymers, for example, proteins and polysaccharides; adjusted regular polymers; manufactured polymers, for example, aliphatic poly (esters) and poly anhydrides.[13]

Mineral Matrices: These comprise of polymers which are gotten from different types of kelp. Illustration is Alginic corrosive which is a hydrophilic sugar acquired from types of chestnut ocean growth (Phaephyceae) by the utilization of weaken alkali.[13]

On the Basis of Porosity of Matrix: 20-23 Matrix framework can likewise be ordered by porosity and thus, Macro permeable; Micro permeable and Non-permeable frameworks can be identified[14-16].

1. Macro porous Systems: In such frameworks the dissemination of medication happens through pores of lattice, which are of size extent 0.1 to 1 µm. This pore size is bigger than diffusant atom size.

2. Micro porous System: Diffusion in this sort of framework happens basically through pores. For small scale permeable frameworks, pore size reaches between 50 – 200 A°, which is somewhat bigger than diffusing atoms size.

3. Non-porous System: Non-permeable frameworks have no pores and the particles diffuse through the system networks. For this situation, just the polymeric stage exists and no pore stage is available.

Polymers used in matrix tablet:
The accompanying polymers are used[17-18]

Hydrogels: Polyhydroxy ethylemethylacrylate (PHEMA), Cross-connected polyvinyl liquor (PVA), Cross-connected polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA)

Table no 1. Patents on Matrix Tablet Technology.

Sr No	Patent No.	Inventor	Title	Type of Matrix	Ref. no
1	WO/2011/008183	RN Prykhodko, *et al*	Trimetazidinedihydrochloride- containing medication in the form of an extended-release matrix tablet (variants) and methods for preparing same (variants)	Hydrophilic	23
2	WO/2011/061616	K. Rajesh K, *et al*	Extended release compositions containing tolterodine and process for preparing the same	Fat-wax	24
3	WO/2011/157730	S. Federico, *et al*	S. Federico, *et al*	Hydrophobic	25
4	JP2011/084577	F. Thomas	Extended release tablet formulation containing pramipexole or pharmaceutically acceptable salt thereof, method for manufacturing the same and use thereof	Bio-degradable	26
5	JP2009185051	GE Amidon, *et al*	Sustained-release tablet comprising reboxetine	Bio-degradable	27
6	WO/2008/001151	G. Jain, *et al*	Controlled release compositions of divalproex sodium	Hydrophilic	28
7	EP1789024	E. Mathiowitz, *et al*	Controlled regional oral delivery	Biomucoadhesive	29
8	WO/1984/004674	CG Jang, *et al*	Dry direct compression compositions for controlled release dosage forms	Fat-wax matrix	30
9	WO/1995/020377	Allen, V. Loyd, *et al*	Rapidly dissolving oral dosage form	Porous matrix	31
10	WO/2006/089215	MA Brandley, *et al*	Pharmaceutical compositions and methods	Floating matrix	32

Table no 2. Drug to be formulated as a matrix tablet with polymer and method used for its preparation:

DRUGS USED	CATEGORY	METHOD USED	POLYMER USED
Zidovudine	Anti-viral	Direct Compression	HPMC-K4M, Carbopol-934, EC
Venlafexine	Anti-depressant	Wet Granulation	Beeswax, Caranuaba wax
Ambroxol HCL	Expectorent, Muco-lytic	Direct Compression	HPMC-K100M
Domperidone	Anti-emetic	Wet Granulation	HPMC-K4M, Carbopol-934
Alfuzosin	Alfa-adrenergic Agonist	Direct Compression	HPMC-K15M, Eudragit-RSPO
Minocycline	Antibiotic	Wet Granulation	HPMC-K4M, HPMC-K15M, EC
Ibuprofen	Anti-inflammatory	Wet Granulation	EC, CAP
Metformin HCL	Anti-diabetic	Direct Compression	HPMC-K100M, EC
Propranolol HCL	Beta-adrenergic blocker	Wet Granulation	Locust bean gum, HPMC
Furosemide	Anti-diuretic	Direct Compression	Guar gum, Pectin, Xanthan gum
Acarbose	Anti-diabetic	Direct Compression	HPMC, Eudragit
Aceclofenac	Anti-inflammatory	Wet Granulation	HPMC-K4M,K15M, K100M,E15,EC, Guar gum
Losartan potassium	Anti-hypertensive	Direct Compression	HPMC-K100M, HPMC-K4M, Eudragit-RSPO
Metoclopromide	Anti-emetic	Direct Compression / Wet Granulation	HPMC, CMC, EC, SSG
Miconazole	Anti-fungal	Direct Compression / Wet Granulation	Pectin, HPMC
Naproxen	Morphine antago-nist	Direct Compression	HPMC-K100M, HPMC-K15M, PVP
Nicorandil	Ca+2 channel blocker	Wet Granulation	HPMC, CMC, EC
Ondansertan	Anti-hypertensive	Wet Granulation	HPMC-K100M, HPMC-K4M, HPMC-K15M
Phenytoin Na	Anti-epileptic	Wet Granulation	Tragacanth, Acacia, Guar gum, Xanthan gum
Ranitidine HCL	H2 antagonist	Direct Compression	Chitoson, Carbopol-940
Theophylline	Respiratory depres-sant	Direct Compression	Carbopol-934P, HPMC-K100M, HPMC-K4M, HPMC-K15M, EC
Tramadol	B2 blocker	Wet Granulation	HPMC-K4M, Karaya gum, Carrageenam gum
Verapemil	Ca+2 channel blocker	Direct Compression	HPMC-K100M, HPMC-K4M, HPMC-

Solvent polymers: Polyethylene glycol (PEG), polyvinyl liquor (PVA), Poly vinyl pyrrolidone (PVP), Hydroxy propyl methyl cellulose (HPMC)

Biodegradable polymers: Polylactic corrosive (PLA), Polyglycolic corrosive (PGA), Poly caprolactone (PCL), Polyanhydrides, Polyorthoesters

Non-biodegradable polymers: Polyethylene vinyl acetic acid derivation (PVA), Polydimethylsiloxane (PDS), Poly-ether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetic acid derivation (CA), Ethyl cellulose (EC)

Mucoadhesive polymers: Polycarbophil, Sodium carboxymethyl cellulose, Polyacrylic corrosive, Traga-canth, Methyl cellulose, Pectin

Natural gums: Xanthan gum, Guar gum, Karaya gum, Locust bean gum.

Technique for Preparation of Matrix Tablet[17, 19]:

A. Wet Granulation Technique:

The process involves the following steps: a. processing and gravitational blending of medication, b. polymer and excipients, c. Planning of fastener arrangement, d. Wet massing by expansion of fastener arrangement or grinding dissolvable, e. Screening of wet mass, f. Drying of the wet granules, g. Screening of dry granules, h. mixing with grease and disintegrant to produce "running powder" Pressure of tablet.

B. Dry Granulation Technique:

This processing involves the following steps: a. processing and gravitational blending of medication, b. polymer and excipients, c. Pressure into slugs or move compaction, d. Processing and screening of slugs and compacted powder, e. Blending with oil and disintegrant, f. Compression of tablet.

C. Sintering Technique:

Sintering is characterized as the holding of nearby molecule surfaces in a mass of powder, or in a reduced, by the utilization of warmth. Traditional sintering includes the warming of a smaller at a temperature underneath the liquefying purpose of the strong constituents in a controlled domain under air weight. The adjustments in the hardness and deterioration time of tablets put away at raised temperatures were depicted as an aftereffect of sintering. The sintering process has been utilized for the creation of managed discharge framework tablets for the adjustment and hindrance of the medication discharge.

Mechanism of drug release from matrix tablet[20-22]:

Drug in the outside layer exposed to the bathing solution is dissolved first and then diffuses out of the matrix. This process continues with the interface between the bathing solution and the solid drug moving toward the interior. It follows that for this system to be diffusion controlled, the rate of dissolution of drug particles within the matrix must be much faster than the diffusion rate of dissolved drug leaving the matrix. Derivation of the mathematical model to describe this system involves the following assumptions:

a) A pseudo-steady state is maintained during drug release.

b) The diameter of the drug particles is less than the average distance of drug diffusion through the matrix.

c) The bathing solution provides sink conditions at all times. The release behaviour for the system can be mathematically described by the following equation:

$$DM/dh = Co.\ dh - Cs/2 \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where, dM = Change in the amount of drug released per unit area.

dh = Change in the thickness of the zone of matrix that has been depleted of drug.

Co = Total amount of drug in a unit volume of matrix.

Cs = Saturated concentration of the drug within the matrix.

Additionally, according to diffusion theory:

$$dM = (Dm.\ Cs / h)\ dt \quad \ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Where, Dm = Diffusion coefficient in the matrix.

h = Thickness of the drug-depleted matrix.

dt = Change in time.

By combining equation 1 and equation 2 and integrating:

$$M = [Cs.\ Dm\ (2Co - Cs)\ t]\ ½ \quad \ldots\ldots\ldots\ldots\ldots\ldots (3)$$

When the amount of drug is in excess of the saturation concentration then:

$$M = [2Cs.Dm.Co.t]\ 1/2 \quad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Equation 3 and equation 4 relate the amount of drug release to the square-root of time. Therefore, if a system is predominantly diffusion controlled, then it is expected that a plot of the drug release vs. square root of time will result in a straight line. Drug release from a porous monolithic matrix involves the simultaneous penetration of surrounding liquid, dissolution of drug and leaching out of the drug through tortuous interstitial channels and pores. The volume and length of the openings must be accounted for in the drug release from a porous or granular matrix:

$$M = [Ds.\ Ca.\ p/T.\ (2Co - p.Ca)\ t]\ 1/2 \quad \ldots\ldots\ldots\ldots\ldots (5)$$

Where, p = Porosity of the matrix

t = Tortuosity

Ca = solubility of the drug in the release medium

Ds = Diffusion coefficient in the release medium.

T = Diffusional path length for pseudo steady state, the equation can be written as:

$$M = [2D.Ca\ .Co\ (p/T)\ t]\ ½ \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (6)$$

The total porosity of the matrix can be calculated with the following equation:

$$p = pa + Ca/\varrho + Cex / \varrho ex \quad \ldots\ldots\ldots\ldots\ldots\ldots (7)$$

Where, p = Porosity.

ϱ = Drug density.

pa = Porosity due to air pockets in the matrix.

ϱex = Density of the water soluble excipients.

Cex = Concentration of water soluble excipients.

For the purpose of data treatment, equation 7 can be reduced to:

M = k. t 1/2 …….. (8)

Where, k is a constant, so that the amount of drug released versus the square root of time will be linear, if the release of drug from matrix is diffusion-controlled. If this is the case, the release of drug from a homogeneous matrix system can be controlled by varying the following parameters:

- Initial concentration of drug in the matrix
- Porosity
- Tortuosity
- Polymer system forming the matrix
- Solubility of the drug.

Conclusion:

This survey article has been on the origination of sustained or controlled release matrix tablets. Merits and Demerits and Many polymers used to technique such arrangement. Overhead discussion infers that Matrix tablets are useful to conquer the patient consistence and effectiveness of dosage form in evoking desired therapeutic related issues connected with the conventional dosage forms Cost effectiveness and once-day by day dosage are the in addition to focuses alongside different advantages. Subsequently, sustained and controlled release matrix tablets patterns towards the advancement of the dosage form design.

References:

1. Brahmankar DM, Jaiswal S.B. Biopharmaceutics and Pharmacokinetics, A Treatise. 1st edn, Vallabh Prakashan. 335-356,(2005).
2. Lippincot Wiliams and Wilkins Remington. The science and practice of pharmacy, 21st edn, vol-1, 229-938,(2005).
3. Mc Conville JT. Recent trends in oral drug delivery. Dru Del Re Autumn / winter. 2005; 24-26.\
4. Robinson Joseph R.Controlled-Release Drug-Delivery Systems, Chapter-27, Remington: The Science and Practice of Pharmacy, Lippincott Williams and Wilkins, 20th Edition,Vol. 1 903-905,(2002).
5. Chein Y.W. Novel drug delivery Systems. 2nd edn, Marcel Dekker, 139-196,(2002).
6. Kumar S.Matrix Tablets as Controlled drug delivery systems. Indo American Journal of Pharmaceutical Research. 2011;1(4): 343-350.
7. Lachman L, Lieberman HA, Kanig Joseph L. The theory and practice of Industrial pharmacy. Varghese publishing house, 3rd ed, 1990; 346.
8. Harland RS. Drug-polymer matrix swelling and dissolution. *Pharm Res* 1988; 5: 488-94.
9. Kumar Kiran S. Matrix Tablets as Controlled drug delivery systems. Indo American Journal of Pharmaceutical Research. 2011; 1(4): 343-350.
10. Sayed I.Preparation and comparative evaluation of sustained release metoclopramide hydrochloride matrix tablets. Saudi Pharmaceutical Journal. 2009;17:283-288.
11. Chandran S.Design and evaluation of Ethyl Cellulose Based Matrix Tablets of Ibuprofen with pH Modulated Release Kinetics. Indian Journal of Pharmaceutical Sciences. 2008; 70(5): 596–602.
12. Patra Chinam N. Design and evaluation of sustained release bilayer tablets of propranolol hydrochloride. Acta Pharm. 2007; 57: 479–489.
13. Siepmann J.HPMC matrices for controlled drug delivery: new model combining diffusion, swelling and dissolution mechanisms and predicting the release kinetics. Pharm Research. 2000; 16: 1748-1756.
14. Higuchi T. Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. Journal of Pharmaceutical Sciences. 1963; 52: 1145-1149.
15. Suvakanta D. Kinetic modelling on drug release from controlled drug delivery system. Acta Poloniae pharmaceutical and drug research.2010;67(3):217-223.
16. Shruti C. Release modulating hydrophilic matrix systems of losartan potassium: Optimization of formulation using statistical experimental design. European Journal of Pharmaceutics and Biopharmaceutics.2007; 66:73–82.
17. Vyas SP, Khar RK. Controlled Drug Delivery: Concepts and Advances. Ist ed. vallabh prakashan. 2002:156-189.
18. Borguist P.A model for the drug release from a polymeric matrix tablets-effect of swelling and dissolution. Journal of Controlled Release. 2006; 113: 216-225.
19. Vyas SP, Khar RK. Controlled Drug Delivery Concepts and Advances. 1st ed., New Delhi: Vallabh Prakashan. 2010:1-12.
20. Borguist P.A model for the drug release from a polymeric matrix tablets-effect of swelling and dissolution. J Controlled Release. 2006; 113: 216-225.
21. Nishihata T.Overall mechanisms behind matrix sustained release (SR) tablets prepared with hydroxypropyl cellulose. Journal of Controlled Release. 1995; 35: 59-66.
22. Siepmann J.HPMC matrices for controlled drug delivery: new model combining diffusion, swelling and dissolution mechanisms and predicting the release kinetics. Pharm Research. 2000; 16: 1748-1756.
23. RN Prykhodko.Trimetazidine dihydrochloride- containing medication in the form of an extended-release matrix tablet (variants) and methods for preparing same (variants). WO2011008183, assigned to

Tatyana Leonidovna; 2011.
24. R Kshirsagar. Extended release compositions containing tolterodine and process for preparing the same. WO/2011/061616, assigned to M/s Lex Orbis (Intellectual Property Practice); 2011.
25. S Federico.Process for the preparation of controlled release tablet. WO/2011/157730, assigned to C. Colombo ang. via Appiani (Corte del Cotone); 2011.
26. F Thomas.Extended release tablet formulation containing pramipexole or pharmaceutically acceptable salt thereof, method for manufacturing the same and use thereof. Japanese Paten. JP2011084577, assigned to Aisin Seiki Co Ltd; 2011
27. GE Amidon.Sustained-release tablet comprising reboxetine. Japanese Patent JP2009185051, assigned to Pharmacia Corporation; 2009.
28. GE Amidon. Sustained release tablet comprising pramipexole. EP2172199, assigned to Pharmacia Corporation; 2010
29. E Mathiowitz. Controlled regional oral delivery. EP178902, assigned to Spherics, Inc.; 2007
30. CG Jang. Dry direct compression compositions for controlled release dosage forms. WO/1984/004674, assigned to Jang Choong Gook; 1984.
31. Allen, Loyd.Rapidly dissolving oral dosage form. WO/1995/020377, assigned to Janssen Pharmaceutica, Inc; 1995.
32. Brandley MA. Pharmaceutical compositions and methods. WO/2006/089215, assigned to Glaxo Group Ltd; 2006