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Review Article

Past Work Done on the Matrix Tablets: A Quick Reference for the Research Beginner in Sustained-release Dosage Forms

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ABSTRACT

Matrix tablets are also referred to as sustained-release, controlled-release, or prolonged-release extended-release tablets, which will prolong the duration of the release of drug content into the systemic circulation. This work was to collect matter about polymers so far tried in making matrix tablets. Due to the prolonged duration of release, this may increase the bioavailability of the drug. They are made with various polymers, starting with cellulose, its derivatives, and plant gums or mucins. This data was obtained by viewing to peer-reviewed journals and magazines. These tablets can be prepared by direct compression of a blended mixture containing polymers, blending agents, glidants, and other additives. The blend was made as granules and compressed as tablets. The matrix tablets are sustained drug release forms and show better action. The study revealed that the matrix tablet is a simple method for extending drug release for a prolonged period.

Keywords: Drug, Gums, Literature, Matrix, Mucilage, Release.

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INTRODUCTION

Dosage Forms (DF) are the drugs that deliver drug molecules to specific sites of action within the body. Oral DFs include pills, tablets, capsules, syrups, powders, buccal films; and so on.[1] The classification of oral DFs is mainly based on the route and physical form of the drug molecule. Among the various DFs, oral DFs are the most convenient.[2] It is the most straightforward method. It is the best option among the various DFs, and these are the most highly preferred DFs among all the DFs. Oral DFs have many advantages. These DFs have different mechanisms of action in their release.[3] The oral systems are available as tablets, capsules, suspensions, emulsions, lozenges, pills, solutions, etc.

Merits of oral DFs

The virtues are as follows:[4,5]

- Available in various DFs.
- Drugs are readily available by prescription.
- Economical.
- The most natural and easiest drug-giving route.
- Oral routes are less objectionable than parenteral routes.
- require only minimal training for administration.
- Safe.
- Simple and convenient to use.
- Suitable for patients of all ages.
- Toxicity is lagged owing to their delayed onset in their effect.
- Various DFs are available.

Shortcomings of oral DFs

The main pitfalls include:[6]

- Dosages are mostly arbitrary, and titration to the clinical endpoint is impossible.
- In some cases, these medications cause gastric irritations and infections, and sometimes they may lead to a gastric ulcer.
- Late onset of action because it takes time for complete absorption.
- Not a better choice for children and infants.

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- Not suitable for emergencies or for patients who are unconscious.
- Not suitable for patients who are suffering from malabsorption.
- Not suitable for patients who suffer from chronic disorders.
- Patient non-compliance.
- The duration of action may extend into the post-treatment period.
- The level of sedation cannot be altered.

These drugs are not suitable for patients who are suffering from gastrointestinal disorders such as diarrhoea, gastric ulcers, constipation, hyperacidity, constipation, etc.

In these oral DFs in drug is unvaryingly blended in the inert solvent. Matrix polymers are mainly available as swellable hydrophilic polymers and non-swellable hydrophobic polymers. In hydrophilic polymer matrices, the drug molecule will be dispersed in the hydrophilic solvents, and then it hydrates into the gel layer over the tablet surface. This gel layer serves as a barrier against drug diffusion and stops excessive water from entering the tablet; more hydration may result in a thicker layer; balance is achieved by swapping out the inner core of the tablet with the dissolved outside thick gel layer. Non-ionic soluble ethers [HPMC K4M, K15M, HEC]. Water-soluble natural gums [xanthan gum, locust bean gum, and Karya gum]. The drug molecule will be dissolved in hydrophobic solvents in hydrophobic polymer matrices. Examples of hydrophobic polymers are waxes, fatty acids/esters/alcohols, glycerides, etc. The extended discharge of drug is owing to the network passages between the drug and polymer.

USES OF MATRIX TABLETS

Amebiasis

Entamoeba histolytica causes amoebic diseases, which are parasite illnesses that mostly affect the intestine and liver. Matrix Tablets (MT) are used to treat these conditions.Matrix tablets are used in the handling of amoebic disorders, which are parasitic infections that majorly affect the intestine and liver and are caused by Entamoeba histolytica.

Bacterial vaginosis

MT are used to prevent the growth of bacteria in the vagina, which is primarily impacted by Lactobacillus species. Matrix tablets are used to inhibit bacterial growth in the vagina, which is mainly affected by species of Lactobacillus.

Prostatitis

Prostatitis, or bacterially-induced swelling of the prostate gland, is treated with MT. Matrix tablets are used in the handling of prostatitis, which means swelling of the prostate gland hindered by bacteria like *Escherichia coli, Pseudomonas*, and *Enterococci*.

Trichomoniasis

Trichomonas vaginalis-related sexually transmitted diseases are treated with MT. Matrix tablets are used in the dealing of sexually transmitted disorders caused by Trichomonas vaginalis.

Urinary Tract Infections

MT are mostly used to treat bacteria such *E. coli, P. aeruginosa, Enterococci*, and *K. pneumoniae* that cause cystitis. Matrix tablets are mainly used to treat bacteria that cause urinary tract infections like cystitis caused by *E. coli, Pseudomonas aeruginosa, Enterococci*, and *Klebsiella pneumoniae*.

Side effects

- A missed dose or an overdose may cause some problems.
- Drug resistance.
- Impaired liver functions.
- Toxicity of neurons (convulsions, meningitis, peripheral neuropathy).
- Pregnant or breastfeeding women should avoid this product.
- It can sometimes cause a drop in blood cell count (leukopenia, thrombocytopenia, bone marrow aplasia).
- Tendinitis and tendon rupture.

EVALUATION OF MATRIX TABLETS

Some evaluation methods-friability test, uniformity of weight, and hardness test should be performed for the evaluation of tablets according to British pharmacopoeia. By using vernier callipers dimensional tests are performed on tablets. The formulation blend was studied for flow properties before they were compressed into tablets.[7,8]

FLOW PROPERTIES

Angle of Repose (AR)

The force inherent in loose powder can be determined using the AR. It is clarified as the largest possible angle between the surface of the granule pile and the horizontal plane. More powder will slide down the pile's sides if more is added, doing so until the surface angle created by the gravitational force and particle friction is equal. The AR was calculated using Newman's funnel

method. A funnel was used to pour the mixture through, and it could be raised vertically to raise the cone to its highest point (h). The AR was determined using the following formula after measuring the heap's radius (r) (e.q.1).

$$\tan\theta = \frac{h}{r} \text{ --- (1)}$$

Where, θ = AR; h = Height of the cone; r = Radius of the cone base.

Bulk Density

It is described as "weight per unit volume." Pb is calculated by dividing the mass of the particle by the bulk volume. The key elements that affect a powder's bulk density are the spreading of particle sizes, the form of the particles, and their propensity to adhere to one another. There are two types of bulk densities. The arrangement of the particles results in a light powder with a low bulk density because there are large voids between the surfaces of the particles. Because the smaller particles in this situation slip between the large particles, the result is a heavy powder with a high bulk density. The bulk density has a significant impact on the size of containers needed for the handling, delivery, and storage of raw materials and mixtures. It is also necessary for size blending machines. The mixture's apparent bulk density was calculated after being poured into a graduated cylinder (Pb). Calculations were made for the bulk volume (Vb) and powder weight (M) (e.q.2).

$$Pb = \frac{M}{Vb} \quad \text{--- (2)}$$

Where, P_b= Bulk Density; M = Weight of sample in gm; V_b= Final volume of blend in cm^3.

Tapped Density

It is the proportion of the powder's overall mass to its tapped volume. The powder was tapped 500 times to determine the volume. The tapping was repeated and the volume of each tap was recorded (e.q.3).

$$Pt = \frac{M}{Vt} \quad \text{--- (3)}$$

Where, Pt= Tapped Density; M= Weight of the sample in gm; Vt= Tapped volume of blend in cm^3.

Compressibility Index (CI) and Hausner's Ratio (HR)

The CI and HR ⊥are the simple, rapid, and effective methods for estimating powder flow assets. The CI has been proposed as an indirect measure of bulk density of materials because all of these variables may affect the measured CI. To determine the CI and HR, the bulk volume and tapped volume of a powder are measured.

The fundamental procedure is measuring the powder's unsettled apparent volume (V_0) and final tapped volume (V_f) after tapping the substance until no more volume changes occur. The process for calculating the CI and HR varies in some ways. As seen below, the HR and CI are calculated (e.q. 4 and 5).

$$CI = \frac{\text{Tapped density}}{\text{Bulk density}} \text{ X100 --- (4)}$$

$$HR = \frac{\text{Tapped density}}{\text{Bulk density}} \text{ -- (5)}$$

EVALUATION OF TABLETS

The manufactured MT's overall appeal, thickness, hardness, weight fluctuation, friability, and medication amount were evaluated.

General Appeal

The prepared tablets were spherical, white, and of a rounded shape. They had no chips or cracks and were uniformly smooth.

Hardness test

Affords necessary to break a tablet is known as hardness (diameter-based crushing strength). A tablet's strength can be determined by its hardness. The tablet must maintain its stability while being handled and transported mechanically. The level of hardness varies depending on the different tablet types and manufacturers. Hardness can be more than $4kg/cm^2$. A Monsanto tester was used to gauge the hardness.

Uniformity of weight

Periodically reviewing this vital in-process quality control test is required (every half an hour). During compression, the tablets underwent adjustments. Any variation in the weight of the tablet causes under medication or overmedication. Therefore, each batch of tablets should weigh the same amount. The 20 tablets were all individually weighed. The average weight was determined using the combined weight of all pills. The average weight and the individual weights were compared. The % difference between the weight variations should be within the permissible range (7.5%). (e.q.6).

$$\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \text{ X10 -- (6)}$$

Table 1: Plant gums/mucilage for making MT.

Drug	Polymer	References
Albendazole	Guar Gum (GG), Xanthan Gum (XG), and dextrin gum	Kohri *et al.*, 1999.[9]
Flubiprofen	Hydroxy Propyl Methyl Cellulose (HPMC)	Park *et al.*, 1999.[10]
Nifedipine	GG and XG	Yan *et al.*, 2000.[11]
Ambroxol HCl	XG	Heinanen *et al.*, 2001.[12]
Ibuprofen	HPMC	Paradkar *et al.*, 2003.[13]
Diltiazem HCl	Methacrylic acid, Ethyl Cellulose (EC)	Shimpi *et al.*, 2004.[14]
Glipizide	Olibanum gum and HPMC	Patel *et al.*, 2005.[15]
Amoxicillin	HPMC and GG	Patel *et al.*, 2007.[16]
Nimodipine	HPMC	Kale *et al.*, 2008.[17]
Propranolol HCl	XG, Karaya Gum (KG)	Hu *et al.*, 2009.[18]
Ciprofloxacin	Sida acuta gum, kondagogu gum and chitosan	Nithiyananthan *et al.*, 2009.[19]
Aceclofenac	*Prunus americana* gum	Shah *et al.*, 2010.[20]
Tramadol HCl	Gum copal and gum dammar	Deore *et al.*, 2010.[21]
Aceclofenac	XG	Katteboina *et al.*, 2010.[22]
Indomethacin	KG and *Terminalia elliptica* gum	Mokarram *et al.*, 2010.[23]
Ropinirole	GG	Stocchi *et al.*, 2011.[24]
Repaglinide	Carrageen gum and bhara gum	Prajapati *et al.*, 2011.[25]
Flutamide	Glucires gum and badam gum	Jyothi *et al.*, 2011.[26]
Metformin	Irvingia gabonensis gum	Garud *et al.*, 2012.[27]
Biguanide	*Grewia mollis* gum	Dilamian *et al.*, 2013.[28]
Ketotifen fumarate	HPMC and XG	Prasad *et al.*, 2013.[29]
Quetiapine fumarate	GG and tara gum	Naral *et al.*, 2013.[30]
Diclofenac sodium	Tamarind gum	Hundekar *et al.*, 2014.[31]
Fluvastatin	Neem gum	El-Helw *et al.*,2015.[32]
valsarton	GG and XG	Zhao *et al.*, 2015.[33]
Labetalol HCl	Polyox, EC, and sodium alginate	Kumar *et al.*, 2016.[34]
Felodipine	XG, pectin, and cashew gum	Jing *et al.*, 2016.[35]
Licozinat	Glycine, L-D methionine	Otgonsuren *et al.*, 2018.[36]
Eplerenone	Aloe vera, GG, and Povidone-k	Ozdemir *et al.*, 2018.[37]
Ivabradine	HPMC K-100, GG, and XG	Sharma *et al.*, 2019.[38]
Glibenclamide	Locust bean gum and KG	Chellappan *et al.*, 2019.[39]
Lamivudine	GG, XG, and pectin	Ozturk *et al.*, 2019.[40]
Losartan K	XG and GG	Harshitha *et al.*, 2019[41]
Azathioprine	Wheat gluten and dextrin	Aziz *et al.*, 2019.[42]
Dextromethorphan HCl	HPMC and carbopol	Mohamed *et al.*,2020.[43]
Ambroxol HCl	XG and pectin	Hu *et al.*, 2020.[44]
Furosemide	Poly ethylene oxide	Vlachou *et al.*, 2020.[45]
Metoprolol succinate	Polyethene glycol	Shinde *et al.*, 2021.[46]
Ciclopirox olamine	GG	Mahajan *et al.*,2021.[47]
Aceclofenac	HPMC and GG	Singh *et al.*, 2021.[48]
Amoxicillin clavulanate	HPMC and GG	Mancabelli *et al.*, 2021.[49]
Biguanide	GMG	Tang *et al.*,2021.[50]
Ketotifen fumarate	HPMC	Salman *et al.*, 2021.[51]
Glibenclamide	LBG and GG	Arrua *et al.*, 2021.[52]
Ciprofloxacin	Chitosan and KG	Hosseini *et al.*, 2021.[53]

Friability test

Friability is the term used to describe the weight loss of the tablet inside the container or package as a result of the disposal of microscopic particles from the surface. This in-process quality control test is done to confirm that tablets can resists shocks throughout production, handling, transit, and shipment. A Roche friability test was used to gauge the tablets' level of friability. It was rotating at a speed of 25 rpm. Five pills that had each been individually weighed were placed inside the friabilator's chamber. The tablets were subjected to rolling inside the friabilator's chamber where they fell freely. Later on of 4 min, the tablets were

taken and the entire batch of intact tablets was weighed once more (e.q.7).

$$\text{loss on friability} = \frac{(W1 - W2)}{W1} X10 \quad \text{--- (7)}$$

Where, W_1 = weight of the tablets before test; W_2 = weight of the tablets after test.

Plant gums that were tried for making matrix tablets were summarized in Table 1.

CONCLUSION

Matrix tablets have many advantages that make them interesting to use as an oral DF. Matrix tablets help increase the efficacy of the dose and patient compliance. The problem of high production costs, which was a disadvantage in the early days, has been solved with improvements in technology. These tablets improve safety and efficacy when used as an oral sustained-release formulation, but they should not be used for more effective therapies.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

DF: Dosage forms; **HPMC:** Hydroxy Propyl Mthyl cellulose; **HEC:** Hydroxy Ethyl Cellulose; ***E. coli*:** *Escherichia coli*; **CI:** Carr's Index; **HR:** Hausner ratio, **GG:** Guar gum; **XG:** Xanthan gum, **EC:** Ethyl cellulose, **KG:** Karaya gum, **LBG:** Locust bean gum.

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