A Review on Matrix Tablets to Treat Pulmonary Arterial Hypertension

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***Abstract*—Pulmonary arterial hypertension (PAH) is a serious disease of the arteries connecting the heart to the lungs (the pulmonary arteries). As PAH develops, blood flow through the pulmonary arteries is restricted and the right side of the heart is put under increasing strain to pump blood through to the lungs. This leads to the main symptoms of PAH – breathlessness, chest tightness limited exercise capacity and fatigue. Pulmonary Arterial Hypertension (PAH) is a syndrome characterized by a progressive increase in pulmonary vascular resistance leading to right ventricular overload and eventually to right ventricular failure and premature death.**

Matrix tablet as sustained release (SR) has given a new breakthrough for novel drug delivery system (NDDS) in the field of pharmaceutical technology. Hydrophilic polymer matrix is widely used for formulating an SR dosage form.

The aim of drug delivery system is to provide therapeutic amount of drug to appropriate site in the body to achieve immediate therapeutic response and to maintain the desired drug concentration. Sustained release, sustained action, prolonged action, extended action are the terms used to identify drug delivery system that are designed to achieve a prolong therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.

Hydroxy propyl methyl cellulose is widely used in oral, ophthalmic, nasal and topical pharmaceutical formulations. In oral products, hypromellose is primarily used as a tablet binder.

This review primarily provides an overview of the progress of development of novel drug delivery system (NDDS) in the field of pharmaceutical technology and the characterization of matrix tablets evaluation as a quality control to ensure safety and efficacy of drug loaded matrix tablets and designed product meet its intended purpose.

***Index Terms*—PAH, Matrix Tablet, NDDS.**

I. INTRODUCTION

Hypertension is a common condition that occurs when your blood pressure is persistently elevated. It can damage your heart, brain, and other organs. With the symptoms of shortness of breath during exertion, fatigue, chest pain, dizziness, fainting, and swelling in the legs and ankles PAH is a specific type of pulmonary hypertension [1], where the blood vessels in the lungs become thickened and narrowed, making it harder for the heart to pump blood through them [2] [3].

PAH can be effectively treated with modified-release (MR) drug delivery which offers many advantages over conventional dosage forms. Modified release (MR) products also offer several potential therapeutic benefits. The primary benefits that can be achieved are referred to as extended release and delayed release [4]. The benefits of these formulations include:

- Sustained blood level
- Attenuation of adverse effects
- Improved convenience and patient compliance
- Protecting acid-sensitive drugs

MR dosage forms can be separated into two forms: monolithic and multiple unit formulations [5]. Monolithic forms generally entail a simple manufacturing process, as they can be produced using conventional tableting processes. Multiple unit preparations, such as pellets, require a more complex manufacturing process but do provide less variable progression in the gastrointestinal (GI) tract. As such, it's easier to combine components with different drugs or release profiles through the use of pellets [6]. When pellets are in a capsule, the adjustment of the dose can be made without any formulation modification. This is because the mass of the pellets can be modified to contain the correct dosage. The diversity of pellet materials (for example, capsules, sachets or liquid suspension) help to make medicine suitable for multiple patient populations – particularly for those that struggle to swallow whole tablets or capsules [7].

In addition, by using pH-sensitive or time-controlled polymer coatings for pellet formulations, the enteric deliver can be controlled and make the progression of pellets in the GI track less sensitive to variation in comparison to monolithic forms following meal consumption. Pellets also present a lesser chance of dose dumping caused by a bad coating [8].

Types of Modified Release Drug Delivery Form

Several modified forms are described with regards to drug release at the targeted sites, frequency of the administration, bioavailability, nature, onset and duration of action. Consequently, modified released formulation have been devised which fall under the following categories [9].

- EXTENDED-RELEASE DOSAGE FORMS:

A dosage form that allows at least a two-time reduction in dose frequency as compared to the drug presented as immediate release form.

Matrix tablets [10] is an important tool for extended - release dosage forms, extended drug delivery is delivery of drug at a rate or at a location determined by needs of body or disease state over a specified period of time. Matrix tablets are most commonly used methods to modulate the release profile of drugs. They are much desirable and preferred for such therapy because they offer better patient compliance, maintain uniform drug levels, reduce dose and side effects, and increase safety margin for high potency drugs [11]. One of the most common approaches used for prolonging and sustained the rate of drug release is to incorporate a dug in hydrophilic colloid matrix such as beta-cyclodextrin hydroxypropylmethylcellulose (HPMC), eudragit RS100, ethylcellulose, cellulose acetate hydrogen phthalate, guar-gum, microcrystalline cellulose. Recently much emphasis is being laid on the development of matrix sustained formulations such as matrix tablets [12]. 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 [13].

Tablet matrix system containing hydrophobic lipid-based materials have been widely used in formulations for extended drug delivery applications because of their chemical inertness [14], cost effectiveness, regulatory acceptance.

- Sustained release: It includes the drug delivery system that achieves slow release of drugs over an extended period of time not particularly at a predetermined rate [15].
- Controlled Release: The drug delivery system from which the drug is delivered at a predetermined rate over a long period [16].

➢ Release dosage forms: A dosage form that release a discrete portion of drug at a time or times other than promptly after administration, although one portion may be released promptly after administration. Example: Enteric coated dosage form

➢ Targeted release dosage form: A dosage forms that releases drug at the intended physiological site of the action and they may have extended-release characteristics also.

➢ Repeat action dosage forms: It is a type of modified release formulations designed to release one dose of the drug initially followed by a second dose of drug at a predetermined interval.

➢ Prolong action dosage forms: It is designed to release the drug slowly to provide a continuous supply of the drug over an extended period of time [17].

- SUSTAINED RELEASED DOSAGE FORMS

The aim of drug delivery system is to provide therapeutic amount of drug to appropriate site in the body to achieve immediate therapeutic response and to maintain the desired drug concentration. Sustained release, sustained action, prolonged action, extended action are the terms used to identify drug delivery system that are designed to achieve a prolong therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.

The goal of a good drug delivery system is to provide a therapeutic amount of drug to the proper site in the body promptly and maintaining the desired concentration. That is, the drug- delivery system should deliver drug at a rate dictated by the needs of the body over a specified period of treatment [18]. This idealized objective encompasses two aspects most importantly spatial placement and temporal delivery of the drug. Spatial placement relates to targeting a drug to a specific organ or a tissue while temporal delivery refers to controlling the rate of drug delivery to the target tissue.

Advantages of sustained release dosage form

❖ Increase patient compliance.
❖ Avoidance of night time dosing.

- ❖ Reduction in dosing frequency.
- ❖ Reduced fluctuations in circulating drug levels.
- ❖ More uniform effect.
- ❖ Improve bioavailability of some drug [19].
- ❖ Minimize or eliminate some local side effect.
- ❖ Avoid patient compliance problem.

CLASSIFICATION OF MATRIX TABLET:

- Hydrophobic matrices
- Lipid matrices
- Hydrophilic matrices
- Biodegradable matrices
- Mineral matrices

II. CHALLENGES AND FUTURE PERSPECTIVES

Due to the progressive nature, complex pathophysiology, and the need for individualized approaches, effective delivery of medicine is a big challenge to pharmacologists and researchers. But advancements in the diagnosis and management of pulmonary arterial hypertension (PAH) have resulted in significant improvements in outcomes for patients with this devastating and progressive disease.

Pulmonary hypertension (PH) is a complex condition that associates with multiple diseases and may affect several organs beyond the cardiovascular and respiratory systems.

Novel Drug Delivery System (NDDS) provides therapeutic amount of drug to appropriate site in the body to achieve immediate therapeutic response and to maintain the desired drug concentration.

Advantages of Matrix tablets: The New Drug Delivery System provides considerable advantages over conventional drug administration.

- ❖ Reduce the toxicity by slowing drug absorption.
- ❖ The use of sustained release formulations to avoid the high blood concentration.
- ❖ Sustained release formulation may maintain therapeutic concentrations over prolonged periods.
- ❖ Minimize the local and systemic side effects.
- ❖ Improvement in treatment efficacy.
- ❖ Minimize drug accumulation with chronic dosing.
- ❖ Sustained release formulations have the potential to improve the patient compliance.
- ❖ Increase the stability by protecting the drug from hydrolysis or other derivatives change in gastrointestinal tract.
- ❖ Can be made to release high molecular weight compounds [20].

Disadvantages of Matrix Tablet:

- ❖ Preparation of matrix tablet with high cost.
- ❖ The remaining matrix must be removed after the drug has been released.
- ❖ The drug release rates vary with the square root of time. Release rates continuously diminish due to an increase in diffusional resistance and/or a decrease in effective area at the diffusion front. However, a substantial sustained effect can be produced through the use of very slow-release rates, which in much application are indistinguishable from zero order.
- ❖ The released rates are affected by various factors such as, food and rate transit through the gut [21].

Challenges intrinsic to clinical programs in middle- and low-income regions (MLIRs) affect diagnosis and treatment of PH. These challenges range from lack of resources to cost of care, limited expertise, unpredictable availability of medications, and the extremely rare option of lung transplant. The disease spectrum is further complicated by late presentation and coexisting comorbidities (i.e., infections, malnutrition, and hypercoagulability).

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Not Applicable

REFERENCES

[1] McLaughlin, V. V. O. Sitbon, et al. 2005. Survival with first-line bosentan in patients with primary pulmonary hypertension. European Respiratory Journal 25(2): 244-249.

[2] Yen-Chun Lai, Karin C Potoka, Hunter C Champion, Ana L Mora, Mark T Gladwin. 2014. Pulmonary Arterial Hypertension: The Clinical Syndrome. 2014 Jun 20;115(1):115-30. doi: 10.1161/CIRCRESAHA.115.301146.

[3] Paul M. Hassoun, M.D. Pulmonary Arterial Hypertension. December 15, 2021, N Engl J Med 2021;385:2361-2376 DOI: 10.1056/NEJMra2000348.

[4] Nita Mondal. The Role of Matrix Tablet in Drug Delivery System. 2018. International Journal of Applied Pharmaceutics. ISSN- 0975-7058 Vol 10, Issue 1, 2018.

[5] Nikolett Kallai-Szabo, Dora Farkas, Milena Lengyel, Balint Basa, Christian Fleck, Istvan Antal. 2024. European Journal of Pharmaceutical Sciences. Volume 194, 1 March 2024, 106704

[6] Ranjana Chopra, Fridrun Podczeck, J. Michael Newton, Göran Alderborn. 2002. European Journal of Pharmaceutics and Biopharmaceutics. Volume 53, Issue 3, May 2002, Pages 327-333.

[7] A Laicher, W S Fuchs. 1998. Pellet technology. Sustained-release pellets in hard gelatin capsules--a suitable dosage form for theophylline. Arzneimittelforschung, 1998 May; 48(5A):540-7.

[8] Modi, S. A., Gaikwad, P. D. et al. 2012. Sustained release drug delivery system: a review. Int J Pharma. Res Dev 2(12): 147-160.

[9] Andrade, F., M. Videira, et al. 2011. Nanocarriers for pulmonary administration of peptides and therapeutic proteins. Nanomedicine 6(1): 123-141.

[10] J. M. Ghormade 1, S. K. Yadav, P. V. Burakle and A. S. Raut. 2023. The role of matrix tablet in controlled release drug delivery system. GSC Biological and Pharmaceutical Sciences, 2023, 23(01), 220–225.

[11] J. M. Ghormade, S. K. Yadav, P. V. Burakle and A. S. Raut. 2023. The role of matrix tablet in controlled release drug delivery system. GSC Biological and Pharmaceutical Sciences, 2023, 23(01), 220–225

[12] Lordi, N. G. 1986. Sustained release dosage forms. The theory and practice of industrial pharmacy 3: 442-454.

[13] Siepmann, J. and Peppas, N. A. 2001. Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). Advanced drug delivery reviews 48(2): 139-157.

[14] Miyagawa, Y., Okabe, T. et al. (1996). "Controlled-release of diclofenac sodium from wax matrix granule." International journal of pharmaceutics 138(2): 215-224.

[15] Sujit Bose, Amandeep Kaur, S K Sharma. A Review on Advances of Sustained Release Drug Delivery System. 2013. International Research Journal of Pharmacy 4(6).

[16] Singh, B. N. and Kim K. H. 2000. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. Journal of Controlled Release 63(3): 235-259.

[17] Mauludin, R. 2009. Nanosuspensions of poorly soluble drugs for oral administration, Berlin, Freie Universiteit Berlin, Diss., 2009.

[18] Patel, H., Panchal, D. R. et al. 2011. Matrix type drug delivery system: A review. Journal of Pharmaceutical Sciences and Bioscientific Research 1(3): 143-151.

[19] Misra, A., Ganesh, S. et al. 2003. Drug delivery to the central nervous system: a review. J Pharm, Pharm Sci 6(2): 252-73.

[20] Maru, S. M. 2013. Formulation Development of Sustained Release Zidovudine- lamivudine Fixed Dose Combination Pediatric Mini Matrices by Hot Melt Extrusion, University of Nairobi.

[21] Mughal, M. A. 2011. Development and evaluation of sustained release antihypertensive drugs using gums and polymer combinations, university of Peshawar.