Review Article

Dual Release System of Solid Oral Dosage Forms

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ABSTRACT

The dual release system is used to achieve both quick and sustained release effect from dosage form. The dual release action achieve by using core compressed tablet, bi-layer or multi layer tablet, IR and SR granules containing matrix tablet and capsules. Some researcher formulated dual release system by incorporating disintegrants for immediate release part and different polymers for sustained release part. Prodas, Duredas and Madopar are dual drug delivery systems available in market. This systems are evaluate by using parameters like weight variation, thickness, hardness, friability, drug content, *in-vitro* dissolution study, etc.

Keywords: Dual release system, core compressed tablet, bi-layer tablet, immediate release.

INTRODUCTION

The solid oral dosage forms are convenient to use and it is widely used in treatment. The numbers of products based on new drug delivery systems have significantly increased in the past few years.

Dual release systems are designed to release drug at two different rates or in two different periods of time. The one drug is immediate release and other drug or may be same drug is slow release. An immediate release system provides an initial burst of drug release and followed by a constant rate of release over a defined period of time. The immediate release system is used for acute condition and slow release system is used for chronic condition in which dosing frequency is more[1].

Types of Dual Release System

Core Compressed Matrix Tablet[2]

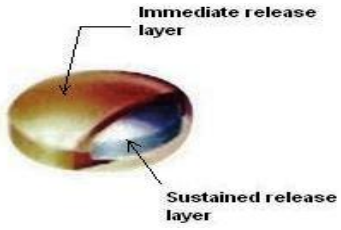

Figure 1: Core compressed matrix tablet

This tablet contain tablet within other tablet. One inner tablet is core tablet and the drug release is slowly from it. Outer tablet is coat tablet and drug release from this site is fast. Two steps employed in core compressed tablet formulation. Separately prepared granules of core and coat tablets are compressed subsequently in compression machine. Core tablet containing sustained release granules are compressed lightly in first steps and then these tablets is placed in centre of die cavity of compression machine containing 40% of granules of coat tablets (immediate release part). Fill up the total die cavity of compression machine with remaining part of granules and core compressed tablet formulated by higher compression force (fig. 1).

Here the therapeutic action of one drug is achieved quickly because the outer coat release drug fast and this action can be achieved by superdisintegrants. Sustained action of other drug can be achieved by using different polymers which can release the drug slowly up to long time by using matrix system. This biphasic release system can be achieved by immediate release coat layer and sustained or controlled action by using polymeric matrix system[3].

Recently, Li and Zhu, using combinations of versatile minitablets (rapid release, sustained release, pulsatile, and delayed onset sustained with various releasing lag times), obtained a multifunctional and multiple-unit oral drug delivery system, including a quick/slow release system.

Bi-Layer Tablets[4,5]

The combination of an immediate release layer and sustained release layer will be in the form of a bi- or multi-layer tablet. In a bilayer tablet, one portion of the tablet contains the drug and other excipients like disintegrants, lubricant, binder, etc in the required dose. The second portion of the tablet will contain drug and polymers which gives sustained release effect of drug.

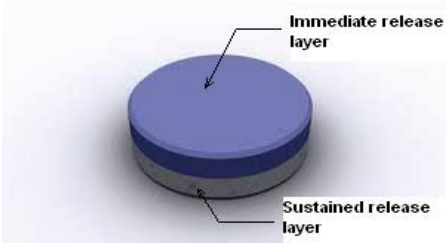

Figure 2: bi-layer tablet

Manufacturing of Bi-Layer Tablets[6]

The manufacture of bi-layer tablets, produced by the sequential compaction of loose powder layers has recently become of increased interest within the pharmaceutical industry due to the tailored release profiles of active ingredients that may be obtained[7]. An observed disadvantage of the formulation however, is the prediction of the assemblies to fail at the interfacial boundary zone between the two adjacent layers.

For preparation of the bi-layer dual release system, the die of the tablet machine fill with sustained release component.

The sustained release component is compress and the fast release powder added to the precompress sustained release component.

The bilayer tablets with two incompatible drugs can also be prepared by compressing two separate layer of each drug and then addition of intermediate inert material can be compressed[8].

Matrix Tablet containing SR Granules & IR Granules[9]

For the prolong release of drug, polymeric materials can be use. The most important characteristics of this type of preparation is that the prolong release may last days & weeks rather than for a shorter duration. The first example of an oral polymeric matrix tablet is Gradumet (Abbott Laboratories), which is marketed as an iron preparation. The plastic matrix provides a rigid geometric matrix surface for drug diffusion so that a relatively constant rate of drug release is obtained**.** One drug is release immediately when goes to stomach due to disintegration. Sustained release drug is achieved due to polymeric material containing granules.

Capsule containing SR Granules & IR Granules

Instead of matrix tablet simple capsule shell is used for fill the SR Granules & IR Granules. The capsule contains granules of both the drug in which one type's granule is for immediate release and other is polymeric for sustained release[10].

Table 1: Dual release system developed by researchers

Author	Formulation	Drug	Excipients Used
Carla Martins Lopes[11]	Matrix Core Tablet	Ibuprofen	Hydroxypropyl methylcellulose and ethylcellulose, Sodium croscarmellose (disintegrant)
G Vijaya Ranga Vittal[12]	Matrix core tablet	Aceclofenac	Hydroxypropyl methylcellulose, ethylcellulose and Xanthan gum, Croscarmellose sodium (disintegrant)
Patel Geeta M.[13]	Bi-layer vaginal tablet	Metoclopramide hydrochloride	Hydroxypropyl methylcellulose K100M and Ucarflock 302, Ac-di-sol (disintegrant)
Hitesh P. Patel[14]	Mini tablets in tablet	Diclofenac Sodium	Hydroxypropyl methylcellulose K100M and Ethyl cellulose, Croscarmellose sodium (disintegrant)
Sree Harsha[15]	Nanospheres	Amoxicillin	Carbopol
Patel Geeta M[16]	Bi-layer tablet	Atorvastatin Calcium and Metoprolol Succinate	Polyox WSR N-60K and Hydroxypropyl methylcellulose K100M, Poloxamer 188
Sahu manoranjan[17]	Matrix Core Tablet	Glimepiride and metformin hydrochloride	Hydroxypropyl methylcellulose and polyvinyl pyrollidine, sodium starch glycolate (disintegrant)
V.Madhusudan[18]	Coating tablet in which coating layer contain one drug	Pseudoephedrine Hydrochloride and Triprolidine Hydrochloride	Gelatin

Technology for Dual Release Dosage Form

PRODAS[19]

PRODAS means Programmable Oral Drug Absorption System developed by Elan Corporation is a multi-particulate drug delivery technology. It formulated by encapsulation of controlled-release mini-tablets which have the size range of 1.5 to 4 mm in diameter. This technology is a combination of multi-particulate and hydrophilic matrix tablet technologies and thus provides the benefits of both these drug delivery systems in one dosage form. The desired release rates can be achieve by using mini-tablets with different release rates incorporated into single dosage form.

The dosage form may contain immediate release and sustained or controlled release mini-tablets. The PRODAS technology may contains targeted drug delivery of specified drug absorption at specific GIT site.

DUREDAS[20]

DUREDAS means Dual Release Drug Absorption System which is formulated by Elan Corporation. It contains bi-layer tableting technology. This technology provides release of drug at two different rates or dual release drug from a single dosage forms. This tablet is formulated by using two different types of granules in which one is for immediate release and other granules utilize for sustained release action. The immediate release part contains disintegrant and sustained release part contains some polymers. The drug release from sustained release part is slow because this polymer may swell in contacting with GI fluid and then drug released for prolong time period. As penetration of fluid into polymeric matrix layer

the drug dissolve and then it absorbed from GIT and sustained or controlled action can achieved. This DUREDAS technology gives immediate and sustained/controlled action of two drugs from single dosage form which contains two layers of two different drug releasing granules.

MADOPAR DR[21]

MADOPAR DR is a l-dopa containg three-layered gastro-retentive matrix tablet which is use for the treatment of Parkinson's disease. The quick onset of effect is achieve by releasing outer layers of the l-dopa in high concentration, whereas the inner sustained release layer is made up of water swellable hydrophilic polymer (HPMC), which swells in the presence of water and increases the gastric retention time of the tablet. The maintenance dose releases slowly up to 6 hours by swelling of tablet.

Evaluation Parameters of Dual Release System

Weight variation[22]

Individually weigh randomly selected 20 tablets and calculate the average weight. The tablets meet pharmacopeal test if not more than two tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit. The weight variation limits for tablets differ depending on tablet average weight.

Thickness[23]

The thickness of tablets is critical to their therapeutic effectiveness. The weight of a compressed tablet is dependent on factors like density, diameter and thickness. In theory, the density of the powder blend and the diameter of the resultant tablet (which is dictated by the die wall) should remain unchanged. The calipers and thickness testers can be used to determine the thickness of tablets. The tablet thickness should be not more than 5% variation to the standard value.

Hardness[22]

The tablets must be hard enough to withstand mechanical stress during packaging, shipment, and handling by the consumer. Hardness is some time termed as tablet crushing strength. The hardness of tablets can be measured by using hardness taster like Monsanto tester, the Strong Cobb, the Pfizer tester, Stokes hardness testers, etc. The principle of testers involves measurement of load to the increasing order until the tablet breaks or fractures. The load is applied along the radial axis of the tablet.

Friability[22]

Tablet hardness is not absolute parameter to check strength because of some formulations compressed in to very hard tablet and produce cap which is lose by attrition. Therefore, another parameter of tablet strength is friability. The friability test is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. In the laboratory friability is usually carried out by the use of the Roche friabilator. A number of tablets are weighed and placed in the plastic chamber of apparatus which operated at 25 rpm speed where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are dusted and reweighed. The percentage weight loss is calculated. The conventional compressed tablets that lose less than 0.5 to 1% of initial weight are generally considered as acceptable.

Drug content[22]

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. For the highly potent drug, 10% limit as labelled amount and for larger dose drug in tablet permits 5% of limit as labelled amount. For content uniformity test, randomly 30 tablets are selected form representative batch and 10 are assayed individually. Nine of 10 tablets must contain not less than 85% or not more than 115% of labelled drug content. The tenth tablet may not contain less than 75% or more than 125%of the labelled content. If this condition is not meet, the remaining tablets must be assayed individually, and none may outside of the 85% to 115% range.

In- vitro Drug Release[24]

In vitro drug release can perform according to the USP. For drug release study paddle type dissolution apparatus is preferable at required rpm speed. A minimum of 6 tablets per batch is required. The dissolution media is 0.1N HCl at a pH 2.0 and a volume of 750 ml for the first 2 hours after which 250 ml of 0.2 M sodium phosphate, tribasic, is add to give a final pH of 6.8 and maintained at 37+ 0.5 ˚C. Test sample (5ml) is withdraw at particular time interval and replace with fresh dissolution media maintained at the same temperature and the concentration. Estimation of the drug can be carried out by using suitable analytical methods.

CONCLUSION

Dual release system has advantage over convention dosage forms. It gives better patient compliance because of immediate and sustain release of drug achieve in single dosage forms so better control over disease condition. Solid dual release system can be successfully formulated as core compressed tablets, bi-layer tablets, immediate and sustain release granule containing tablet or capsules. Immediate release action can be achieve by using various disintegrants and sustain release action can be achieve by some polymers.

Some market products are Prodas, Duredas and Madopar as dual drug delivery systems. The prepared dosage form characterized by weight variation, friability, thickness, hardness, drug content and *in-vitro* dissolution study.

REFERENCES

1. Mithilesh Kumar Jha, Habibur R and Mofizur, Biphasic oral solid drug delivery system: A review, International Journal of Pharmaceutical Sciences and Research, 2(5), 2011, 1108-15.
2. Sowmya C., Reddy S. C., Tabasum S. G., Varma V., An overview on bi-layer tablets, International Journal of Pharmacy & Technology, 4(2), 2012, 2143-56.
3. Conte U., Maggi L., Multi-layered hydrophilic matrices as constant release devices (GeomatrixTM Systems), Journal of Controlled Release, 26(1), 1993, 39–47.
4. Abdul S., Poddar S.S., A flexible technology for modified release of drugs: multi layered tablets, Journal of Controlled Release, 97(3), 2004, 393–405.
5. Inman S. J., Briscoe B.J., Topographic characterization of bilayered tablets interfaces, Chemical Engineering Research and Design, 85(A7), 2007, 1005-12.
6. Inman S. J., Briscoe B.J., Axial tensile fracture of MCC, International Journal of Pharmaceutics, 34(2), 2007, 47-55.
7. Roberts R. J., Rowe R.C., The relationship between the fracture properties, tensile strength and critical stress intensity factor of organic solids and their molecular structure, International Journal of Pharmaceutics, 125(1), 1995, 157–62.
8. Wu C.Y., Best S. M., A simple predictive model for the tensile strength of binary tablets, European Journal of Pharmaceutical Sciences, 25(2), 2005, 331–6.
9. Marshall K., Sixsmith D., Surface geometry of some microcrystalline cellulose, Journal of Pharmacy and Pharmacology, 24, 1972, Suppl: 138P.
10. Aulton M. E., Taylor K., Aulton's Pharmaceutics: The Design and Manufacture of Medicines, 3rd Ed, Elsevier Health Sciences, Churchill Livingstone, 2013, 678-86, 2013.
11. Lopes C. M., Jose M. S., Joao F. P., and Paulo C. C., Compressed Matrix Core Tablet as a Quick/Slow Dual-Component Delivery System Containing Ibuprofen, AAPS PharmSciTech, 8(3), 2007, Article 76.
12. Vittal G V R, Deveswaran R, Bharath S, Basavaraj B V, Madhavan V, Fabrication of matrix core tablet as a bi phasic dual-component delivery system containing aceclofenac, Int J Pharm Bio Sci, 2(1), 2012, 132-8.
13. Patel G. M., Patel M. M., Compressed matrix dual-component vaginal drug delivery system containing metoclopramide hydrochloride, Acta Pharm, 59, 2009, 273–88.
14. Patel H. P., Patel N. J., Formulation and evaluation of biphasic drug delivery system of diclofenac Sodium using compressed mini tablet, International Journal of Pharma Research and Development, 3(1), 2011, 76-83.
15. Sree H., Dual drug delivery system for targeting *H. pylori* in the stomach: preparation and *in vitro* characterization of amoxicillin-loaded Carbopol nanospheres, International Journal of Nanomedicine, 7, 2012, 4787–96.
16. Patel G. M. and Patel D. H., Formulation and evaluation of once a day regioselective dual component tablet of atorvastatin calcium and metoprolol succinate; Int. J. PharmTech Res., 2(3), 2010, 1870-82.
17. Manoranjan S., Formulation of dual component drug delivery of glimepiride and metformin hydrochloride for immediate and sustain release, Int. J. Res Ayurveda and Pharm, 1(2), 2010, 624-33.
18. Madhusudan V. and Rao K. N., dual release drug delivery system as gelatin coated tablets, Global Research & Development, banner pharmacaps, Bangalore, India, 2011.
19. Verma R. K. and Garg S., Current status of drug delivery technologies and future directions, Pharmaceutical Technology On-Line, 25(2), 2001, 1–14.
20. Patel R.R., Patel J.K., Novel technologies of oral controlled release drug delivery system, Syst Rev Pharm, 1, 2010, 128-32.
21. Rathbone M.J., Hadgraft J., Roberts M.S., Modified-Release Drug Delivery Technology, Weimar, Texas 78962. 2003.
22. Lachman L., Lieberman H.A., Kanig J.L., The Theory and Practice of Industrial Pharmacy. 3rd Ed. Mumbai, Verghese Publication House, 1987, 296-301.
23. Shiyani B., Gattani S., Surana S., Formulation and evaluation of bi-layer tablet of metoclopramide hydrochloride and ibuprofen, AAPS PharmSciTech, 9, 2008, 18–27.
24. Prabhakar S., Formulation and evaluation of bilayer tablets of diclofenac sodium with ranitidine hcl for sustained and immediate release, Journal of Applied Pharmaceutical Science, 02(05), 2012, 136-41.

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