Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2019; 11(1): 30-33

ISSN- 0975 1556

Research Article

The Effect of Modified Release Dosage Forms on Absorption of Medications

Heyam Saad Ali[1], Rasha Saad Suliman[2], Babiker M A Elhaj[3], Raina Suliman[4]

[1]Department of Pharmaceutics and Pharmacy Practice, Dubai Pharmacy College, Dubai, United Arab Emirates
[2]College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences Ministry of National Guard Health Affairs, Riyadh, Kingdom of Saudi Arabia
[3]Pharmaceutical Sciences, College of Pharmacy Ajman University of Science and Technology.
[4]College of Sciences, Princess Nourah Bint Abdulrahman University.

Available Online:25th February, 2019

ABSTRACT

Pharmaceutical industries focus on enhancing patients' compliance by reducing dosing frequency and minimizing side effects. People above 40s year are frequently experiencing potential drug-drug interaction during combination therapy poly-therapy of once- daily formulations. The market is progressing rapidly in modified release technological advancements in improving bioavailability of drug delivery systems by controlling the erratic drug-release and plasma-concentration profiles. Consequently, enhancing patient compliance, cost effective and minimizing side effects and toxicities. This review focusing on the classification of different modified release drug dosage forms with their plasma-concentration profiles associated with absorption and changes in controlling and management of diseases.

Keywords: Modified Release drug delivery, absorption, patients' compliance.

INTRODUCTION

Most oral conventional products have immediate release' of drug/drugs from the solid dosage forms as in tablets and capsules. In such delivery systems no modifications to the rate of the release, therefore, rapid drug absorption from the gastrointestinal tract resulted in drug plasma fluctuations due to the increase of dosing frequency and reduction of time interval. Drug fluctuation can be risky, because it may lead to sub-therapeutic or toxic effects. This leads to the need of a drug that has close to a constant level in the blood, hence will enhance patient's compliance and clinical efficacy of the drug for its intended use[1].

Therefore, to overcome these limitations and increase patients' compliance, scientists have utilized modified release technologies on the conventional dosage forms, which resulted in the discovery of the well-known modified release dosage forms[1,2].

Modified release dosage forms are divided mainly into two classes: extended release dosage form and delay release dosage form. In such dosage forms, the rate and extent of drug absorption can be controlled to match the therapy goals in chronic diseases management[3].

Extended release drug products are dosage forms that release the drug slowly upon prolonged period, as compared to the conventional ones. Therefore, they allow extended drug absorption and enhance the rate and extent of drug present in the blood (bioavailability) so that its level in the plasma is within the therapeutic range for longer time. Moreover, reduction in dosing frequency will minimize side effect and enhance patient compliance[4,7]. (See Figure 1)

On the other hand, delayed release drug products are dosage forms that release a portion of drug at a time other than immediately after administration. Enteric-coated dosage forms are commonly classified as one type of delayed release products (e.g. enteric-coated aspirin and other non-steroidal anti-inflammatory products)[3,5].

In delayed release dosage form (Figure 2), the principle is based on pH function, and a tablet is coated with acidic material in order to restrict drug gastric release and allows enteric drug release and dissolution in the small intestine. Such type of formulations is done to either protect the stomach from a potentially irritating drug like Aspirin or protect the drug like Erythromycin from gastric degradation in the acidic medium and allow release and absorption in the intestine[6].

Let us take Aspirin as an example, it is a weekly acidic drug and as what we can expected from Henderson Hasselbalch equation: it will have more of unionized form in the stomach (acidic pH) which means higher lipophilicity to pass through the semipermeable lipid bilayer membrane of the stomach. So hypothetically, it is supposed to be absorbed from the wall of the stomach. Meanwhile, in reality aspirin is absorbed mainly from the intestinal wall not from the stomach. This is all due to the fact that for any drug to get absorbed from the GIT, it should have sufficient hydrophilicity and optimum lipophilicity. That is why Aspirin is formulated in a modified release dosage form (delayed or enteric coated). Such formulations allow aspirin to get absorbed form the intestine through special aqueous channels, carrier

**Author for Correspondence: sulimanr@ksau-hs.edu.sa*

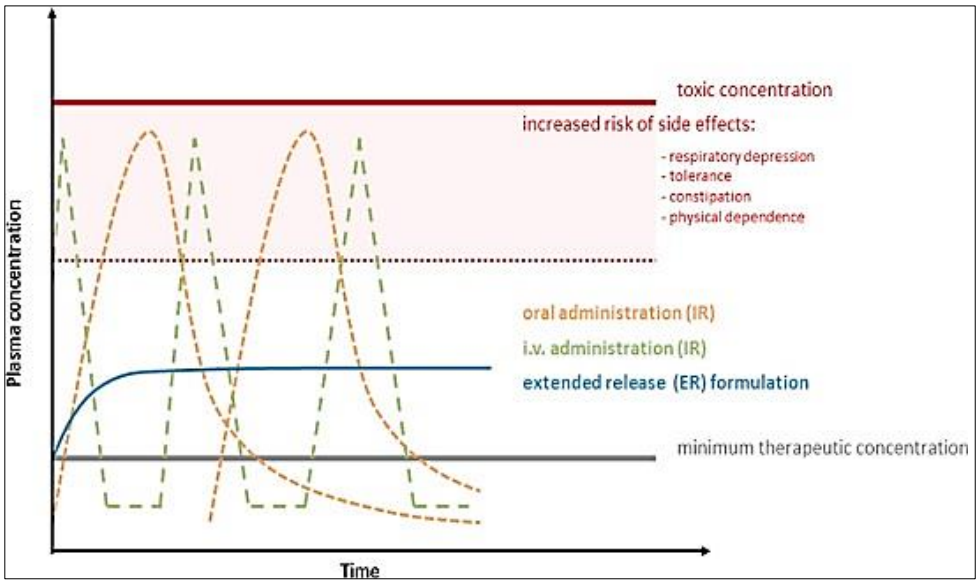

Figure 1: The plasma concentration Vs time; curve represent reduction in dosing frequency will minimize side effect and enhance patient compliance.

Figure 2: An example of acidic drug (aspirin) in an enteric coated tablet.

mediated, ion pairing and in-between the villi of the intestine as it has large surface area and high vascularity[1,7].

$pH = pKa + log\frac{[A-]}{[HA]}$ Henderson Hasselbalch equation

Moving to enteric-coated tablets, which are considered as a type of delayed release products. This type of formulation has a special principle standing behind it, which depends mostly on PH values. Selection of Enteric coating polymers should resist dissolution at PH values below 4: but begin to dissolve at PH equals or more than 5 and become readily soluble at PH 7. The most effective enteric materials are long chain polymers with ionizable groups. In the low pH environment of the gastric fluid of the stomach, the group remains unionized. So that the coating material will remain insoluble while, it will disintegrate or dissolve in the higher pH of the intestine (basic environment) to allow the release of the active drug from the core to the intestine so that absorption through the wall can take place[3,8].

Finally, modified release dosage form fields are becoming a site of interest for most scientists and companies to work on because of the great returns that they can achieve through controlling the rate of release and consequently absorption of medications using the previously explained methods (Figure 3).

Modified-release dosage form

Modified-release dosage form is used to explain the products that change the rate and time of release of a drug substance. They are based on time, course, and/or location intended for therapeutic or patient's convenience, these characteristics are not found in the immediate release formulations[9].

The goal in designing modified release dosage forms

The goal in designing modified release dosage forms is to reduce the frequency of dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required, or providing uniform drug delivery and basically to achieve a steady state drug in blood level for extended periods of time[4,7].

Advantages

Control of drug therapy
Modification of the rate and extent of drug absorption
Reduction of frequent doses
Improvement of patient compliance
Patient's convenience
Enhancing the bio-availability with minimum doses
Increase the safety of highly potent drugs

Disadvantages

Immediate termination of therapy isn't achieved
Dose adjustment may be less flexible
Expensive
Designed on average biological half life

The usual dosage forms of modified release drugs are formulated in tablets and capsules which are packaged and stored in a similar way of the traditional ones. They are also found in ocular, parenteral, sub-dermal and vaginal products[10].

They are of two types

Delayed release: enteric coated tablets or capsules intended to be released in the intestinal tract by passing through the stomach in its unchanged form.

Extended release: products that are in controlled manner at a predetermined rate, duration and location to result in a proper therapeutic blood level of drug.

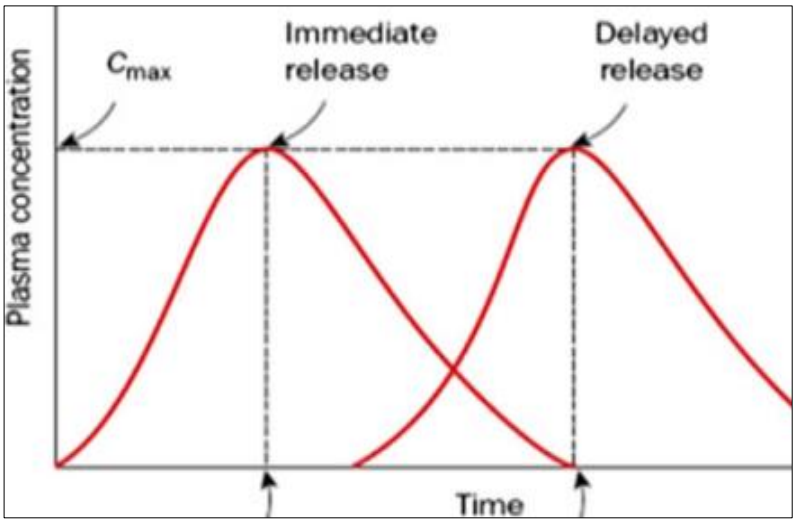

Figure 3: The plasma concentration Vs time; curve represent the effect of the modified release dosage forms in time.

Different Terminologies used in modified release:
Sustained release
Delayed release
Prolonged release
Extended release
Controlled release
Site-specific targeting and receptor targeting
Advantages of modified release formulations[3, 6, 8]
Improved patient compliance and convenience due to reduction in dosing frequency.
Reduction in fluctuation in steady state level and therefore better control of disease condition due to constant plasma drug level over a long period of time.
Minimize the drug accumulation with chronic dosing.
Minimize or eliminate local and systemic side effects.
Maximum utilization of the drug enabling reduction in total amount of dose administered.
Increased safety margin of high potency drugs due to better control of plasma drug level.
Disadvantages of modified release formulations:
Administration of modified release medication does not permit prompt termination of therapy.
The physician has less flexibility in adjusting dosage regimens.
Possibility of dose dumping due to food, physiological or formulation variables or chewing and grinding of oral formulations by the patient and thus increased risk of toxicity.
Poor in-vitro-in-vivo correlation.
More costly process and equipment's are involved in manufacturing SRDFs.
Drugs absorbed at specific sites can't be given in this dosage form[11].
Modified release dosage form examples:
Oral dosage form
Extended release (eg. Controlled release, sustained release, prolonged release)
Delayed release (eg. Enteric coated)
Intramuscular Dosage Forms
Depot injection
Water-immiscible injections (eg. Oil)
Subcutaneous Dosage Forms
Implants
Transdermal Delivery System
Targeted Delivery Systems
Colon targeted
Physicochemical and biological considerations properties related to modified release candidates
Aqueous solubility
Limited Absorption of poorly soluble drug
Partition coefficient
Drugs that are very lipid soluble will result in low and rapid flux into the tissue will lead undesirable accumulation in tissue.
Drug stability
Enteric unstable drugs should not be formulated into prolonged release systems due to sub-therapeutic outcomes.
Protein binding
The extent of protein binding plays an important role in long half-life of elimination for the drug, since it acts as drug reservoir and influences drug delivery.
Molecular size and diffusivity
Diffusivity, is a function of drug molecular size (or molecular weight). It has impact on the polymericsize and shape of diffusing species.
Biological half-life
Drugs with shorter half-life (2-4 hrs) make excellent candidate for sustained release preparation since this can reduce dosing frequency[2, 4, 8, 11].
Biological properties
Absorption
Uniformly released drug from its dosage form could ensure sustained release system and subsequent uniform absorption of the drug.
Distribution
Drugs with high apparent volume of distribution, are considered as poor candidates, since it reduce concentration and amount of drug either in the blood or in the tissues.

Metabolism

Metabolism is considered as the critical element in partial or complete termination of drug biological activity. Therefore, the metabolic patterns is an essential key in making the design of sustained drug delivery system.

Duration of Action

Duration of action of a drug is governed by biopharmaceutical properties and distribution, metabolism and elimination processes which decide drug selection for sustained release formulation.

Side effects

Controlled release formulations can minimize the incidence of side effects by controlling the plasma concentration of the drug e.g. Levodopa has lowered the incidence of side effects[12].

Challenges for formation of modified release systems

Drugs of Low solubility and low permeability [class IV]
Type and concentration of the Polymer used.
Control membrane integrity.
Simulated models adopted in IVIVC correlation studies.
Low Therapeutic window drugs.
Dosage strength/ patient compliance[13].

REFERENCES

1. Davis Yohanes Arifin, Lai Yeng Lee , Chi-hwaWang ; Mathematical Modeling And Simulation Of Drug Release From Microspheres: Implications To Drug Delivery Systems ; Advanced Drug Delivery Reviews 58 (2006) 1274–1325.
2. Sharp J. Good Pharmaceutical Manufacturing Practice. CRC Press, 2005.
3. Griffin JP. The Textbook of Pharmaceutical Medicine. 5th ed. Blackwell Publishing, 2006.
4. Diffusion controlled systems in controlled release of biologically active agents. By john Wiley and sons 1987.
5. Heyam Ali, Rasha Saad, Babiker El-Haj: Prevention of Cap-Locking of Syrup Product by Treating the Manufacturing Process with Citric Acid Monohydrate. International Journal of Pharmaceutical Chemistry. Aug. /2015. 5 (3), 218-226. DOI: 10.7439/ijpc
6. Kamel A.E., Sokar M., Nagger V. & Gamal S.A., Chitosan and sodium alginate-based bio adhesive vaginal tablets, AAPS Pharm Sci., 2002, 4(4): 1-7.
7. Hwang S., Owada E., Suhardja L.H.U.,Flynn G.L. & Higuchi W.I., Systems approach to Vaginal delivery of drug: 4 methodology for determination of membrane surface pH., J Pharm Sci., 1977,66: 778.
8. A.H. Beckett, R.N. Boyes, and E.J. Triggs, J. Pharm. Pharmacol. 20 (2) 92-97 (1968).
9. K.G. Van Scoik, "Solid pharmaceutical dosage in tablet triturate form and method of producing same," US patent 5,082,667 (1992).
10. J.W. Conine and M.J. Pikal, "Special Tablets," in Pharmaceutical Dosage Forms: Tablets, H. A. Lieberman, L. Lachman and J.B. Schwartz, Eds. (Marcel Dekker, New York, NY, 1989), pp. 338-339.
11. Navin Dixit et.al, Sustained Release Drug Delivery System, Indian J of Research in Pharmacy and Biotechnology 2013; 1(3): 305-310.
12. Sathish Ummadi et al,Overview on Controlled Release Dosage Form, International J of Pharma Sciences 2013; 3(4): 258-269. 12. Ansel H.C, Allen L.V, Popovich N.G. Pharmaceutical dosage forms and drug delivery systems. 7th ed; 2000: 230.
13. Rasha Saad, Fadli Asmani, Mohamed Saad, Maryam Hussain, Jiyauddin Khan, Mohammed Kaleemullah, Nordin Bin Othman, Ali Tofigh, Eddy Yusuf: A New Approach for Predicting Antioxidant Property of Herbal Extracts. International Journal of Pharmacognosy and Phytochemical Research 02/2015; 7(1): 166 - 174 .