JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Pulsatile Drug Delivery Systems: Current Scenario

Dr.Upendra Kulkarni*, Sampada H.C, Hariprasanna R.C

RMES's College of Pharmacy, Gulbarga, INDIA

ABSTRACT:

Sustained release or controlled release dosage systems have large advantages over conventional drug delivery systems because of their lesser frequency of dose and controlled release of drug. Pulsatile drug delivery system is one such system which offers controlled release of drug at desired site and on required time. Its accuracy is attributed to circardian rhythm of the body and it releases drug in the form of pulse. The relation between physiology of disease and time along the day is discovered. Drug deliveries in the form of single-unit and multiple-unit systems are developed.

KEYWORDS: Pulsatile Drug Delivery system, Controlled release dosage system, circardian rhythm

Article history:
Received 21 Dec 2012
Accepted 05 Jan 2013
Available online 13 Feb 2013

For Correspondence:

Dr.Upendra Kulkarni

Depapartment of Pharmaceutics

RMES's college of pharmacy

Old jewargi road

Gulbarga, Karnataka, India.

Mobile: +919740311947

Email: upendra613@gmail.com.

INTRODUCTION:

Pulsatile drug delivery systems are gaining importance because of their dependency on circardian rhythm of the body. They provide scope for controlled release dosage form formulation which has significant therapeutic importance. After the study of pulsatile drug delivery, it is becoming increasingly evident that the specific time at which the patients take their medication may be even more significant than was recognized before. To understand the concept of pulsatile drug delivery, it is necessary to define the following terms.

Chronobiology :[1]
It is the term concerned with the study of physiology of diseases according to time. Chrono refers to time and biology refers to study of life.

Chronopharmacology: [1]
It is the study of varying pharmacological effects of drugs with respect to time along the day.

Chronopharmacokinetics: [2]
It is the study of temporal changes in ADME of drugs.

Chronotherapy: [1]
It involves the study of co-ordination between biological rhythm and medical treatment given to a patient.

Graphical representation of pulsatile drug delivery system

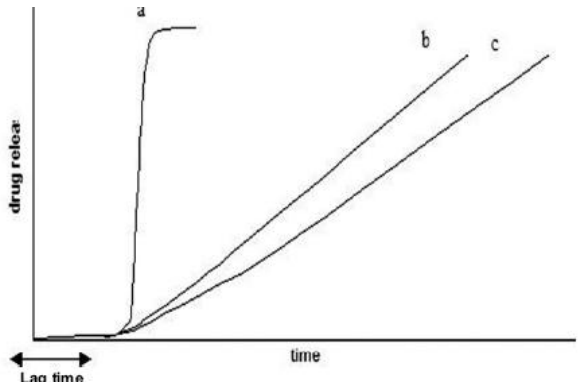

Fig. 1: Drug release profiles from pulsatile drug delivery system a = release of drug as a "pulse" after a lag time, b = delivering the drug rapidly and completely after a "lag time" and c = constant drug release over a prolonged period of time after a "lag time".

Biological rhythms

Biological rhythms can be explained under following classes.

1. Ultradian rhythms
2. Infradian rhythms
3. Circardian rhythms

Ultradian rhythm includes cycles which last for a day. Ex: 90 minute sleep cycle.Infradian rhythm includes cycles which take more than one day for completion. Ex: Menstrual cycle.Circardian rhythms are endogenous oscillations which are self-sustained.

Diseases influenced by chromotherapeutics.

Disease type:	Examples
Neoplastic	Cancers like blood cancer, breast cancer, lung cancer etc.
Inflammatory	Rheumatoid arthritis, asthma etc.
Cardiovascular	Angina pectoris, myocardial infarction, high blood pressure etc.

Description of few diseases based on circardian rhythm.

1. Hypertension:

Blood pressure shows increase in its levels during early morning hours, declines from midday and is least at midnight. Rise in blood pressure in morning hours among hypertensive patients is termed as "a.m" systolic blood pressure.

Circardian variations in blood pressure.

2. Myocardial infarction:

Due to the release of catecholamine, cortisol, increase in platelet aggregation and vascular tone, the occurrence of MI is more in the morning hours.

3. Arthritis

Osteoarthritis patients have minimum pain in morning hours whereas patients suffering from rheumatoid arthritis feel more pain in morning hours. In this situation, taking medication at night is a common solution.

Classification of pulsatile drug delivery systems:

Based on the methodology of formulation, they are classified into single-unit and multiple-unit systems.

Single-unit pulsatile systems:

This system is sub-divided as

a. Capsule based systems
b. Osmotic systems
c. Delivery systems with soluble/ erodible membranes
d. With rupturable coating

a. Capsule-based systems

Capsule-based systems are most common in single-unit systems. The principle is based on swelling of plug which gets moved away to release drug in the form of pulse. A hydrogel plug which can swell is used to seal the drug contents into the capsule body. [3] The capsule, after it comes in contact with the dissolution fluid, the plug swells and is pushed out of the capsule to release the drug. The lag time is controlled by length of plug and the region of insertion into the capsule.

Krogel and Bodmeier [4] studied the release of chlorpheniramine which utilizes capsules fitted with erodible plugs.

Soutar et al. studied the delivery of paracetamol 500mg with a hydrophilic sandwich capsule which was gastroresistant targeted to ileocaecal junction. Tmax of salivary amylase sample was found to be 7.9 hour (SD+/- 0.96) [5].

b. Osmosis based system

The capsule is coated with a semi-permeable membrane. Insoluble plug is inserted into the capsule. The plug consists of osmotically active agent

and the active drug. When this system comes in contact with dissolution fluid, only water is permitted into it and pressure is developed. Due to this pressure, insoluble plug is expelled.

Linkwitz et al. invented osmotic drug delivery capsule. The drug delivery from this was dependant on osmotic infusion of moisture from surrounding environment. It was given with an orifice which would open to achieve pulsatile drug delivery effect. (6)

A similar system was given by Port[R]

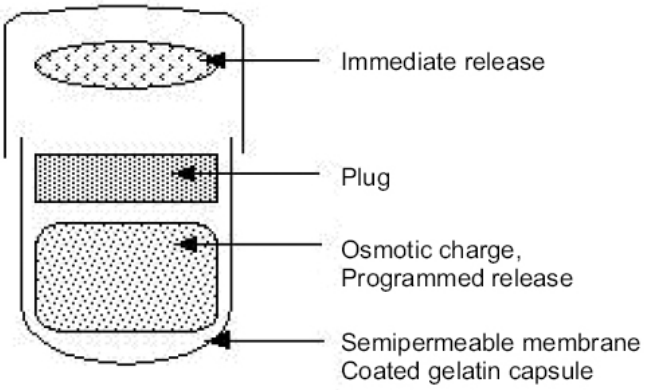

Figure 2: Plan of system

c. Soluble/erodible barrier coating system

In this system, the drug reservoir is surrounded by a soluble barrier layer which dissolves slowly with time. After lag time, the drug is released at once. Chronotropic[R system] consists of a core containing drug reservoir coated with HPMC, a hydrophilic polymer. (7, 8, 9) An additional enteric coated film is given outside this layer to overcome intra-subject changes in gastric emptying rate. (10)

Thickness and viscosity of HPMC decide the onset of action and lag time.

d. Rupturable membrane/coating systems

These systems contain reservoir system surrounded by an outer layer of rupturable membrane. The effervescent agent or swelling agent present in the reservoir causes the layer to rupture because of the pressure.

Bussemer et al. worked on rupturable membrane pulsatile systems where the drug was reserved in hard gelatin capsules. The capsules were coated by a swelling layer and a coat of insoluble and water-permeable substance. When the capsule comes in contact with water, the system took up water and swelling layer swelled and caused outer layer to rupture because of the pressure. It was also concluded that lag time can also be shortened by the addition of HPMC to the outer coating. (11)

Multiple-unit pulsatile systems

Gastric emptying system is more dependable in multiple-unit system when compared to single-unit system. These systems are classified as under:

1. Pulsatile system based on change in permeability

Chen et al. formulated an osmotic multiparticulate drug delivery system for diltiazem. It was formulated to release the drug in divided doses over time intervals to produce pulsatile effects. Hard gelatin capsules were consisting of 3 pellets, each pellet consisting of core containing the active ingredient and water-soluble modulating agent like sodium chloride. Binder used was polyvinylchloride. The coating was made up of water-insoluble and water permeable agent. The thickness of this coat in the three pellets was varied. The first pellet had the thinnest coat, third had the thickest and second had the thickness in between first and third. The rate of release of drug was controlled by thickness of the coat. pH independent materials were used for coating. (12)

2. Pulsatile system with rupturable coating

The system involved in the rupturable coating of single-unit and multiple-unit systems remain same but in multiple delivery units with varied thickness of coatings were formulated. This thickness decides the release rate of the drug. Bai et al. (13) worked on the same principle.

Conclusion

Pulsatile drug delivery systems are gaining popularity because of its advanced drug delivery and patient compliance. These drug delivery systems are especially helpful for patients suffering from chronic hypertension, arthritis and myocardial infarction.

REFERENCES

1. Jha N, Bapat S: Chronobiology and chronotherapeutics. Kathmandu University Med. Jour. 2004; 2(8): 384-388.

2. Vipul P Patel: Pulsatile drug delivery system. A review: PHARMATUTOR-ART-1060.
3. Mc Neill, M.E., Rashid, A. and Stevens, H.N.E., **GBPatent No.,** GB2230442, 1993.
4. Krogel, I. and Bodmeier, R., **Pharm. Res.,** 1998, 15, 474.
5. Soutar, S., Stevens, H.N.E., Mahony, B.O., Bakshee, M., Perkins, A.C., Grattan, T. and Wilson, C.G., **Proc. Int. Symp. Control Release Bioact. Mater.** 2001, 28, 790.
6. Linkwitz, A., Magruder, J.A., Merrill, S., **US Patent No.,** US5318558, 1994.
7. Gazzaniga, A., Ianartino, P., Maffione, G. and Sangalli, M.E., **Int. J. Pharm.,** 1994, 2, 77.
8. Gazzaniga, A.; Sangalli, M.E.; Giordano, F; **Eur J. Biopharm. Pharm.,** 1994, 40, 246.
9. Gazzaniga, A., Busetti, C., Moro, L., Crimella, T., Sangalli, M.E. and Giordano, F., **Proc. Int. Symp. Control Release Bioact. Mater.** 1995, 22, 242.
10. Polli, S., Busetti, C. and Moro, L., **EP Patent No.,** EP0572942, 1993.
11. Bussemer, T., Dashevsky, A. and Bodimeier, R., **J. Control. Release,** 2003, 93, 331.
12. Chen, C.M., **US Patent No.,** US5260068, 1993.
13. Bai. **US Patent No.,** US 5840329, 1998.