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Review Article

## PULSATILE RELEASE OF EPROSARTAN MESYLATE FOR CHRONOTHERAPEUTICAL APPLICATIONS EMPLOYING EXPERIMENTAL DESIGN

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### Abstract

Pulse pressure (PP) is recognized as one of the most important cardiovascular risk factor in older subjects and those with isolated systolic hypertension. The aim of the study was to evaluate the effect of the Angiotensin receptor blocker Eprosartan Mesylate on pulse pressure in patients with isolated systolic hypertension. In chronopharmacotherapy (timed drug therapy) drug administration is synchronized with biological rhythms to produce maximal therapeutic effect and minimum harm for the patient. These systems are designed for diseases showing chronopharmacological behavior and where the drug dose is required for extended day time or night time activity or for the drugs having high first pass effect or having site specific absorption in GIT, or for drugs with high risk of toxicity. This system is aims to release drugs at a programmed pattern i.e.at appropriate time and/or at appropriate site of action. The major challenge in the development of pulsatile drug delivery system is to achieve a rapid drug release after the lag time.

**Keywords:** Pulsatile drug delivery system, Hypertension, Lag time, Eprosartan Mesylate.

### Introduction

A pulsatile drug delivery system is characterized by a lag time that is an interval of no drug release followed by rapid drug release. Pulsatile systems are basically time-controlled drug delivery systems in which the system controls the lag time independently of environmental factors like pH, enzymes, gastro-intestinal motility etc. These time-controlled systems can be classified as single unit (e.g. tablet or capsule) or multiple units (e.g. pellets) systems. These systems are designed according to the circadian rhythm of the body. The multiple unit systems like pellets or mini tablets are preferred for drug dosage forms because the coating of the medicated units can be formulated to trigger the release in order to comply with the release profile of a pulsatile design [1,2,3,4,5].

It is thought that clinically effective plasma drug concentrations of an antihypertensive medicine, in the early morning, would maximize a drug's effect on blood pressure during that period. Paradoxically, waking to

take such a drug in the early morning might induce the morning surge in blood pressure that the drug is designed to prevent. Thus, a formulation with a lag time before drug release might achieve the desired drug concentration profiles [6,7,8,9].

A variety of such systems has been proposed over the last two decades and the simplest system is the matrix device where the drug is dispersed within a polymer network. The device may be swellable, hydrophilic, erosion controlled or non-erodible. The latest advances propose the development of more complicated systems in order to improve or adjust the release of the drug in a required time and manner. These can be multilayer systems, core in cup systems and compressed coated systems. Multilayer tablets comprise an active layer containing a matrix core and one or more barriers, applied during tableting. Core in cup systems usually release drug from a constantly eroding surface as the impermeable cup prevents drug release from the lateral

surface. Compressed coated systems completely surround the core with different polymeric barrier-layers. These coatings prevent drug release from the core until the polymeric shell is entirely eroded, dissolved or removed. The delay in drug release depends primarily on covering of the device and secondarily on the core composition. Several systems exhibit a lag time that is dependent on the coating properties. The lag time is frequently followed by a release phase and this characteristic is indicative of pulsatile drug delivery. Combinations of the above devices could be used to further control or modify the release rate of a drug [10,11,12,13,14,15,16,17].

## Conclusion

We conclude that Eprosartan Mesylate is an effective and well tolerated antihypertensive drug able to reduce PP in patients with isolated systolic hypertension. This reduction is partially independent of the severity of high blood pressure. This aspect may be important in terms of safety and target organ protection. Pulsatile drug delivery system can effectively tackle this problem as it is modulated according to body's circadian clock giving release of drug after a specified time lag. A significant process has been made toward achieving pulsatile drug delivery system that can effectively treat diseases with non-constant dosing therapies. Various technologies are researched and some are currently in the market.

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