Magda S Sokar, Pharmaceut Anal Acta 2014, 5:3
http://dx.doi.org/10.4172/2153-2435.S1.021

OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference and Exhibition on
Pharmaceutics & Novel Drug Delivery Systems
March 24-26, 2014 Hilton San Antonio Airport, San Antonio, USA

Valsartan time-clock pulsatile tablet formulations preparation and *in vitro* evaluation

Magda S Sokar
Alexandria University, Egypt

The time-clock system is a system having a lag time independent of the gastric residence time, intestinal enzymes, and mechanical action of stomach or gastrointestinal pH. The aim of the present study was to prepare valsartan (val.) time-clock pulsatile tablets to release valsartan after certain lag time, independent of the gastrointestinal pH, in its absorption window to cope with the circadian rhythm of human body for blood pressure elevation. Core tablets were prepared by direct compression of a homogenous mixture of valsartan, Avicel PH101, Croscarmellose sodium (CCNa), magnesium stearate & Aerosil®.

The core tablets were then sprayed coated with a sealing layer formed of ethyl cellulose (EC) that was subsequently coated with a release-controlling layer. Three different aqueous dispersions namely; carnauba wax (CW) or beeswax (BW) or a mixture in a ratio of 2.5:1, respectively were used to form five time-clock tablet formulations having the release controlling layer with different thickness {B5, B10, B20, BW5 & CW5}. Quality control testings were carried out to the core tablets. Differential Scanning Calorimetry (DSC) was also performed to detect the possible drug excipient interaction in the core tablet formulation. The release was carried out, for the prepared time-clock tablet formulations, in 0.1 N HCl for the first 2 h, followed by phosphate buffer (pH 6.8) for 4.5 h. The effect of pH on valsartan release was studied through a release study in 0.1 N HCl for 6.5 h. Two-phase dissolution study was performed to the selected time-clock tablet formulation to predict the drug permeation through the gastrointestinal tract (GIT). Stability study of the selected formula was performed at 25°C & 60% RH and at 40°C & 75% RH for 3 months.

The results showed that a release-controlling layer composed of a mixture of CW & BW in a ratio of 2.5:1 showed a reasonable release lag time. The release lag time of the tablets increased with the increase of the coat thickness, thus B20>B10>B5 with corresponding lag time values of 4.5, 3 & 2.5 h, respectively. Selected B5 tablet formula exhibited a reasonable lag time after which the highest & complete % drug releases at pH 6.8 was obtained. In addition, a good partitioning of val. between the aqueous and organic phases in a ratio of 1:7 was observed. The selected formula was stable for at least 3 months under standard long-term and accelerated storage conditions. In conclusion, *in vitro* studies revealed that the time-clock system could be used successfully to deliver valsartan in a pulsatile pH-independent manner. It provided a desirable lag time followed by a rapid and complete drug release accompanied by an expected effective permeation through the biological membranes upon release in the duodenum; the window of absorption, as indicated by the two phase release study.

smagda@ymail.com