Introduction

All functions in human being are well controlled in time as biological rhythms of varied periods, both in health and disease. The circadian rhythm has been most explored and shown the great importance to the practice of medicine and chronotherapy. Chronotherapy is particularly significant when the symptoms of disease show a discrepancy predictably over time as epitomized by hypertension, asthma, allergic rhinitis, arthritis, peptic ulcer, myocardial infarction, congestive heart failure and stroke. The application of circadian rhythm to chronotherapy may be accomplished by the pertinent timing of dosage forms to synchronize drug concentrations to rhythms in disease activity. With the progression of knowledge in the field of chronopharmacology, current drug delivery approaches have been elevated to a new concept of chronotherapeutics. As more is learned about chronotherapeutics, it is becoming increasingly more evident that the medication intake time may be even more considerable than was recognized in the past (Sajan et al., 2009). From these points of view, development of dosage forms, in which drug is released only at required time and effective drug levels are maintained, has been desired for chronotherapy. Development of chronomodulated drug delivery system is an approach to fulfill the need for chronotherapy. Various technologies like time-controlled (Ueda et al., 1994), site specific (Soni et al., 2011), gastro retentive (Jagdale et al., 2009), pulsed (Kikuchi et al., 1997) and programmed drug delivery devices (Nayak et al., 2009) have been developed and widely studied in recent years for chronotherapeutic drug delivery.

The two disease conditions share a common core pathophysiology, that is, inflammation of the lower airways in asthma and upper airways in allergic rhinitis (AR). Moreover, both exhibit a remarkably similar temporal pattern in occurrence or exacerbation of their respective symptoms (Smolensky et al., 2007). Asthma is one of the most common diseases with the largest circadian variation (Jha and Bapat, 2004). The symptoms of asthma include dyspnea (difficulty in breathing), wheezy chest, and croupy cough. In patients with asthma, symptoms generally worsen during the early hours of the morning and pulmonary function often deteriorates at the same time (Nainwal, 2012; Smolensky et al., 2007), also the symptoms of allergic rhinitis such as sneezing, nasal rhinorrhea, red itchy eyes, nasal pruritus and nasal congestion was found to occur most recurrently before breakfast in the morning and least frequently in the middle of the day, suggesting a role for chronotherapy (Smolensky et al., 2007).
Co-existence of asthma with allergic rhinitis and their shared pathophysiology have led to the concept of “one airway, one disease” and the need for a common therapeutic approach. To achieve optimal treatment for patients, it is the recommendation of the Allergic Rhinitis and its Impact on Asthma (ARIA) workshop group in collaboration with the World Health Organization (WHO) that patients with persistent AR should be evaluated for asthma, and that patients with asthma should be evaluated for rhinitis. A strategy combining the treatment of both upper and lower airway disease in terms of efficacy and safety appears to be optimal. Montelukast sodium (MKS) a leukotriene receptor antagonists (LTRAs) considered as a useful common therapy to treat both asthma and allergic rhinitis, with clinical evidence for their efficacy and tolerability (Pawankar, 2003; Lane, 1998).

Several drug delivery technologies based on physical and/or chemical activation for chronomodulated drug release that is intended for oral route of administration have been reported (Mandal et al., 2010; Bussemmer et al., 2003; Lecomte et. al., 2003; Fan et al., 2001; Gazzaniga et al., 1994). Among emerging chronotherapeutic approaches, pulsatile drug delivery systems (PDDS) has attracted increasing interest among academic and industrial researchers for its ability to liberate medication following a programmed lag phase (Lin and Kawashima, 2012). Pulsatile drug delivery systems are mostly reservoir type surrounded with a barrier layer. The outer barrier layer can dissolve, erode or rupture on exposure to gastrointestinal (GI) fluid after a certain lag time and drug is released rapidly from the inner reservoir core. The rupturing of the outer barrier layer is induced by an expanding core upon water ingress through the barrier layer. A reservoir system, surrounded by a polymeric membrane which either erodes/dissolves (Gazzaniga et al., 1994; Wilding et al., 1994) or ruptures (Bussemmer et al., 2003; Krogel et al., 1999) has been reported to delay or create the lag period in drug release. The expansion can be caused by effervescent excipients or swelling agents (Mandal et al., 2010; Sunghongjeen et al., 2004). Fan et al., (2001) used blends of ethyl cellulose, EC (GIT-insoluble polymer) and eudragit L (enteric polymer) to coat cross-linked polyvinyl pyrrolidone based Diltiazem HCl containing tablets (Lecomte et. al., 2003). Soni et al., (2011) attempted to achieve the chronotherapy for bronchial asthma by utilizing dual approach for the effective colonic delivery of theophylline using pH dependent solubility behavior of eudragit and susceptibility of guar gum to colonic environment. Yassin et al., (2012) designed a chronotherapeutic delivery system of theophylline with high potential benefits in treating nocturnal asthma.
Several other systems based on capsular drug delivery device have been designed to control the lag time and/or drug release onset which delivers therapeutic agents into the body in a time or position controlled pulsatile release fashion. These systems mainly consist of an insoluble capsule body, housing a drug and a plug (Krogel et al., 1998). A swellable hydrogel plug is used to seal the drug contents into the capsule body. The lag time is controlled by a plug which is pushed away by swelling/erosion and the drug is released as a “pulse” from the insoluble capsule body. Pulsincap is one of such system which is capable of releasing its drug at a predetermined time (Krogel et al., 1998). Nayak et al., (2009) has modified this technology, the hydrogel plug has been replaced by an erodible tablet, which has a tight fit in the capsule to prevent entry of fluid. Tekade and Gattani, (2010) has developed a dual cross-linked beads further coated by eudragit L & S 100 in the ratio 1:2 w/w in order to achieve desired lag time for chronotherapy of asthma. Dual cross linked beads were prepared by dropping dispersed phase of theophylline, delonix-regia gum, and sodium alginate into the calcium chloride solution followed by aluminium chloride solution. Khan et al., (2010) has developed alginate and chitosan beads of theophylline for colon targeted delivery. These pH dependent beads were prepared by inotropic gelation method followed by enteric coating with eudragit S 100.

A comprehensible approach for fruitful appraisal and optimization of the formulation parameters is necessary. Response surface methodology (RSM), supported by statistical software, is most popular approach in recent years for pharmaceutical product development and optimization allowing extraction of complete information out of few well-designed experiments. Central composite design (CCD), one of the techniques in RSM allows investigation with the least number of experiments and selection of the optimal composition for achieving the presetting target (Hao et al., 2012). In present study, we have performed experiments as per CCD, a statistical tool for better understanding of effect of factors and interactions between the factors on responses.

Presently montelukast sodium is available in market as conventional immediate release film coated tablets. It is indicated for the treatment of asthma, exercise induced bronchoconstriction and for the relief of allergic rhinitis. As the marketed formulation releases the drug immediately within an hour of intake. So, there is a need for chronomodulated drug delivery system of montelukast sodium, which will lag the drug release till mid night and then releases the drug, which will take care of asthma as well as allergic rhinitis.