1. Introduction:

Oral controlled drug delivery systems offer temporal and spatial control over the release of drug. Such systems represent the most popular form of controlled drug delivery for the obvious advantage of oral route of drug administration. The spatial targeting of the drug to the colon generally follows pulsatile release. Pulsatile release profile is characterized by the initial lag time followed by the rapid and complete drug release.

![Drug release profile of pulsatile drug delivery system.](image)

In this context, the aim of the research was to achieve a so-called ideal sigmoidal release pattern (pattern A in Figure 1). The characteristic feature of the formulation was a defined lag time followed by a drug pulse with the enclosed active quantity being released at once. Thus, the major challenge in the development of pulsatile drug delivery system is to achieve a rapid drug release after the lag time. Often, the drug is released over an extended period of time means delayed release after initial lag time (patterns B & C in Figure 1). Pulsatile drug delivery system is desirable for the drugs acting or having an absorption window in the gastro-intestinal tract or for the drugs with an extensive first pass metabolism Ex, B-blockers or for the drugs, which develop biological tolerance, where the constant presence of drug at the site of action diminishes the therapeutic effect or for drugs with special pharmacokinetic features designed according to the circadian rhythm of human. Pulsatile drug delivery system is generally classified into time controlled and site specific controlled systems. The release from the former group is primarily controlled by the system while the release in the second group is primarily controlled by the biological environment in the GIT such as pH or enzyme (Gothoskar et
Delivery of drugs to colon has been extensively investigated during the last decade. A number of diseases such as Crohn's disease, Ulcerative colitis, Irritable bowel syndrome and carcinoma of colon can be treated by local delivery of drugs. Colon targeting is also been used for systemic absorption of peptides, oral vaccines, growth hormones, interleukins, insulin as colon provides friendly environment which may be due to lower activity of proteases. Various diseases that exhibit diurnal rhythms may also be treated by using colon specific formulations. Colonic drug delivery can be achieved by oral or rectal administration. With regard to rectal route, the drugs do not always reach the specific sites of the colonic diseases and the sites of colonic absorption. The system can be achieved by various techniques such as pH triggered approach, time dependent approach, pressure dependent approach, microbially controlled delivery, osmotic controlled approach, prodrug approach and bioadhesive system (Mandal et al., 2010; Bussemer et al., 2001; Vyas et al., 2002).

Inflammatory bowel disease (IBD) is an umbrella term which includes Crohn's disease and ulcerative colitis. IBD can be seen most frequently in the early adult life. Most widely used classes of drugs for the therapy include 5-amino salicylic acid (5-ASA) drugs, steroids and immunosuppressant -long term therapy (Aggarwal et al., 2008). All these classes are potent enough but are not devoid of side effects. For example 5-ASA drugs causes anemia, skin rashes, heart burn, reduced sperm count during therapy and are to be taken in high doses. Corticosteroids are associated with hypertension, diabetes, insomnia, osteoporosis, muscle weakness, delayed healing, peptic ulcers, glaucoma, growth retardation, psychiatric disturbances and weight gain while immunosuppressant cause bone marrow suppression, blood problems, kidney and liver damage (Aggarwal et al., 2008). In order to treat these diseases various natural non steroidal anti-inflammatory agents are used.

Strategies for colon-specific drug delivery:

a) Prodrugs:

Prodrug is pharmacologically inactive derivative of a parent drug molecule that requires spontaneous or enzymatic transformation in vivo to release the active drug (Haeberlin et al., 1993; Youan et al., 2004). For colonic delivery of drugs, prodrugs are designed to undergo minimal absorption and hydrolysis in the tracts
of the upper GIT and undergo enzymatic hydrolysis in the colon, thereby releasing the active drug moiety from the carrier (Jing et al., 2008; Dusel et al., 1986). A number of other linkages susceptible to bacterial hydrolysis specifically in the colon have been prepared where the drug is attached to hydrophilic moieties like amino acid, glucuronic acid, glucose, galactose, cellulose, coating materials over drug cores (Yang et al., 2002) etc.

b) pH-Dependent system:
The pH-dependent systems exploit the generally accepted view that pH of the human GIT increases progressively from the stomach (pH 1-2 which increases to 4 during digestion), small intestine (pH 6-7) at the site of digestion and it increases to 7-8 in the distal ileum. Polymers used for colon targeting, however, should be able to withstand the lower pH values of the stomach and of the proximal part of the small intestine and also be able to disintegrate at the neutral of slightly alkaline pH of the terminal ileum, preferably at the ileocecal junction (Vidyasagar et al., 2002).

c) Time-dependent system:
It has also been proposed as a means of targeting to the colon. To attain colonic release, the lag time should equate the time taken for the system to reach the colon (Hebden et al., 1999). This time is difficult to predict in advance, although a lag time of five hours is usually considered sufficient, given that small intestine transit time is reported to be relatively constant at three to four hours (Hebden et al., 1999). A number of systems have been developed based on this principle, with one of the earliest being somewhat complex Pulsincap® device (Wilding et al., 1993).

d) Microflora-activated system:
The bioenvironmental inside the human GIT is characterized by the presence of complex microflora especially the colon that is rich in microorganisms that are involved in the process of reduction of dietary component or other materials (Hovgaard et al., 1996). Drugs that are coated with the polymers, which are showing degradability due to the influence of colonic microorganisms, can be exploited in designing drugs for colon targeting (Sinha et al., 2001).