**Introduction:**

The development of Mini-tablets-filled-capsule systems offer benefits for the production of a sustained release multiple unit dosage form. Mini-tablets are tablets with a diameter equal to or smaller than 2-3 mm. This system has specific advantages over conventional single unit dosage forms. Advantages of multiple unit dosage forms such as Mini-tablet-in capsule systems include a lower risk of dose dumping, less inter and intra such variability and a high degree of dispersion in the digestive tract, thus minimizing the risks of high local drug concentrations.

Oral drug delivery represents by far the most common & convenient way of drug delivery. The gastro-Intestinal tract is still the route of choice for drug administration & absorption.

Chronopharmaceutics is a branch of pharmaceutics devoted to design and evaluation of drug delivery system that release a bioactive agent at a rhythm that ideally matches the biological requirement of a given disease therapy. Ideally chronopharmaceutical drug delivery system (ChrDDS) should embody time controlled and site specific drug delivery system. Evidence suggests that an ideal ChrDDS should:

- Be non-toxic within approved limits of use,
- Have a real-time and specific triggering biomarker for a given disease state.
- Have a feed-back control system (ex: self-regulated and adaptive capability to circadian rhythm and individual patient to differentiate between awake-sleep status),
- Be easy to manufacture at economic cost and
- Be easy to administer to patients and enhances compliance to dosage regimen.

When treating human diseases, the overall goal is to cure or manage the disease while minimizing the negative impact of side effects associated with therapy. In this respect, chronopharmaceutics will be a clinically relevant and reliable discipline if
pharmaceutical scientists could delineate a formal and systemic approach to design and evaluate drug delivery system that matches the biological requirement.

Chronotherapeutics refers to a clinical practice of synchronizing drug delivery in a manner consistent with the body’s circadian rhythm including disease states to produce maximum health benefit and minimum harm. Asthma is a chronic obstructive lung disease characterized by airways, inflammation and hyper-reactivity. In most patients, the condition worsens at night with acute exacerbation being most common.

Circadian variation in pain, stiffness and manual dexterity in patients with osteo and rheumatoid arthritis have been studied and has implication for timing antirheumatide drug treatment. Morning stiffness associated with pain at the time of awakening is a diagnostic criterion of the rheumatoid arthritis and these clinical circadian symptoms are supposed to be outcome of altered functioning of hypothalamic–pituitary–adrenocortical axis.

Chronopharmacotherapy for rheumatoid arthritis has been recommended to ensure that the highest blood levels of the drug coincide with peak pain and stiffness. This drug delivery system that can be administered at night (before sleep) but that release drug in early morning would be a promising chronopharmaceutic system.

Flurbiprofen [1,1’-biphenyl]-4-acetic acid, 2-fluoro-alpha-methyl-, is an important analgesic and non-steroidal anti-inflammatory drug (NSAID) also with antipyretic properties whose mechanism of action is the inhibition of prostaglandin synthesis. It is used in the therapy of rheumatoid disorders. Flurbiprofen is rapidly eliminated from the blood, its plasma elimination half-life is 3-6 hours and in order to maintain therapeutic plasma levels. The drug must be administered approximately 150-200mg daily by oral in divided doses.

The aim of this work is to develop & evaluate the extended release drug delivery of mini-tablets-filled-capsule systems using various water soluble & insoluble polymers like Hydroxypropyl methyl cellulose, Microcrystalline cellulose,
Sodium croscarmellose, ethyl cellulose etc. and flubroprofen as the model drug for its chronotherapeutic delivery whose physicochemical properties and short half life make it suitable candidate for controlled drug delivery system.

**Advantages:**

Many body functions that follow circadian rhythm. A number of hormones like rennin, aldosterone, and cortisol show daily fluctuations in their blood levels. Circadian effects are also observed in case of pH and acid secretion in stomach, gastric emptying, and gastro intestinal blood transfusion.

Diseases like bronchial asthma, myocardial infarction, angina pectoris, rheumatic disease, ulcer, and hypertension display time dependence. Sharp increase in asthmatic attacks during early morning hours, such a condition demands considerations of diurnal progress of the disease rather than maintaining constant plasma drug level. A drug delivery system administered at bedtime, but releasing drug well after the time of administration (during morning hours), would be ideal in this case. It is true for preventing heart attacks in the middle of the night and the morning stiffness typical of people suffering from arthritis.

Drugs that produce biological tolerance demand for a system that will prevent their continuous presence at the biophase, as this tends to reduce their therapeutic effect.

The lag time is essential for the drugs that undergo degradation in gastric acidic medium (e.g., peptide drugs) irritate the gastric mucosa or induce nausea and vomiting. These conditions can be satisfactorily handled by enteric coating, and in this sense enteric coating can be considered as a pulsatile drug delivery system.

Targeting a drug to distal organs of gastro-intestinal tract (GIT) like the colon requires that the drug release be prevented in the upper two-third portion of the GIT. The drugs that undergo extensive first pass metabolism (b-blockers) and those that are characterized by idiosyncratic pharmacokinetics or pharmacodynamics resulting in reduced
bioavailability, altered drug/ metabolite ratios, altered study state levels of drug and metabolite, and potential food-drug interactions require delayed release of the drug to the extent possible.