Chapter 3

THEORETICAL ANALYSIS

Chronotheurapeutics refers to a treatment method in which *in-vivo* drug availability is timed in relation to our body’s natural rhythms (circadian rhythms) to produce maximum health benefits. It is becoming increasingly evident that some medications may work better if their administration is coordinated with day-night patterns and biological rhythms. For example, researchers have reported that asthma is worst in the early morning hours between 4 a.m. to 6 a.m., when cortisol levels in the body are low and histamine concentrations are at their highest level.

In such circumstances chronotheurapeutics plays a prominent role, where the intention is that the formulation is administered in the evening, which provides treatment for disease in which symptoms are experienced in the early morning hours. The principal advantage of chronotheurapeutic pharmaceuticals is to provide optimum plasma levels of drug, resulting in maximum health benefits and minimize the undesired ones. As a consequence there is reduction of dose requirement and this is likely to improve the patient compliance.

In the present study an attempt is made to develop chronotheurapeutic formulations containing anti-asthmatic drugs (Theophylline anhydrous and Terbutaline sulphate). Instead of normal trial and error method, a standard statistical tool of optimization technique is adopted to identify the potential contribution of various formulation variables in the development of chronotheurapeutic formulations for anti-asthmatic drugs.
3.1 Objectives

The following objectives are conceived for the development of dosage forms
★ Selection of various polymers and excipients by using suitable screening design.
★ Development of dosage forms by using suitable experimental designs.
★ To carry out the various in vitro studies for the dosage forms.
★ Application of statistical optimization technique for the development of optimal formulation.
★ To study the in vivo behavior of optimal formulations by using suitable animal model.

3.2 Plan of research work

1. Pre-formulation parameters
✓ Selection of drug candidates based on Physico-chemical and biopharmaceutical parameters.
✓ Development of analytical procedures
✓ Drug excipients compatibility studies
✓ Selection of polymers and excipients by applying screening design.

2. Formulation and In vitro evaluation
✓ Development of dosage forms (PCT & CR tablets) by the application of response surface methodology design of experiments
✓ To carry out the In vitro evaluation of formulations
✓ To carry out the In vitro drug release profiles

3. Optimization and stability studies
✓ Development of polynomial equations
✓ Application of numerical optimization technique for the selection of optimal formulation
✓ Validation of optimal formulation
✓ To carry out the stability studies as per ICH guide lines

4. In vivo studies
✓ To carry out the pharmacokinetic studies by using rabbit as animal model
✓ In vitro-In vivo correlation