# CHAPTER I

# INTRODUCTION

Acyclovir (9-(2- hydroxyethoxymethyl)guanine) is a nucleoside analogue of guanosine which shows effectiveness againt herpes simplex virus type I and II, varicella zoster virus, Eptein-Barr virus and cytomegalovirus (O'Brien and Campoli-Richards, 1989 and Wagstaff et al., 1994). The principal problem with oral acyclovir is its short plasma half-life (2-3 hours) and low bioavailability (Wagstaff et al., 1994), requiring five times daily dosage regimen. This is the major problem in terms of patient compliance, and also means that therapeutic coverage is reduced during night-time hour. Moreover, no commercial oral sustained release product of acyclovir is available. Consequently, it is very interesting to develop oral acyclovir sustained release formulation in order to improve patient compliance due to a reduced frequency of administration and to maintain the drug blood level over the minimum effective levels during both day- and night-time hours.

Among the various methods to formulate sustained release pharmaceutical products, the hydrophilic matrix system is becoming an interesting method to prepare sustained release dosage form for oral administration because of its convenience and easiness of manufacture (Talukdar, 1996). Hydrophilic matrices are composed of drug, hydrophilic polymer and other excipients for controlling drug release. When such a device is exposed to an aqueous medium, i.e., dissolution medium or gastrointestinal fluid, the polymer swells and formation of a protective gelatinous layer controls the drug release from the matrices (Korsmeyer et al., 1983 and Langer and Peppas, 1981). Drug release from hydrophilic matrix is known to be a complex interaction between swelling, diffusion and erosion (Bonferoni et al., 1993 and Colombo et al., 1995).

In this study, the oral acyclovir sustained release tablet was developed by using hydrophilic matrix system. The release profile characteristics of the matrices containing different hydrophilic polymers were investigated. The formulation variables affecting drug release from these matrices were also examined, e.g.

polymer content in the matrices and the type of diluents employed to prepare the matrices. In addition, the effects of pH and ionic strength of the dissolution medium on drug release profile were evaluated.

**Objectives of the study**

1. To investigate sustained release characteristics of acyclovir matrices containing hydroxypropyl methycellouse, xanthan gum, sodium alginate and carbopol 934P as release-retarding hydrophilic polymer
2. To study the effect of different diluents: lactose and dibasic calcium phosphate, in the formulation on sustained release properties of the matrices
3. To examine the effects of pH and ionic strength of dissolution media on sustained release characteristics of matrices
4. To estimate the swelling and erosion properties of matrices in various dissolution media
5. To assess the mechanism of drug release from matrices in different formulations and conditions of dissolution media