PREFACE

Since **Dr.Tsuneji Nagai of Hoshi University, Japan** used the concept of bioadhesion in the early 1980's for the delivery of insulin across the buccal mucosa in beagle dogs; several researchers tried a large number of drugs for administration through buccal mucoadhesive dosage forms. The potential of these dosage forms have been found to be tremendous because of their ability to improve the bioavailability of many such drugs by bypassing the hepatic first pass metabolism. The growing number of newer molecules in the form of peptides and proteins, the research in this field has gained the centre stage for the non-invasive drug delivery.

Diltiazem, the drug in the present investigation is widely used in the chronic treatment of angina pectoris, to control the blood pressure and cardiac arrhythmias. The pain accompanying is very severe. Since unstable angina occurs mostly nocturnally at a time when a person is at rest, the condition is more fatal because the patient cannot get any quick assistance. Diltiazem exhibits very low oral bioavailability due to extensive first pass metabolism in the liver. Though parenteral administration can overcome this limitation, its small biological half-life necessitates its repeated administration making it the least preferred by the patients for chronic usage as an alternative to parenteral route.

In the earlier approaches for the delivery of Diltiazem, conventional matrix tablets, films, patches, discs, microspheres, bilayered systems, ointments and hydrogel systems based on the principle of bioadhesion were developed. Many pre-clinical and clinical studies on various formulations through buccal route have demonstrated that efficacy can be achieved systemically. However, these suffer from some serious drawbacks such as slow onset of action, non-unidirectional drug release, and histological damage to buccal mucosa, incapability of masking bitterness of drugs or lack of retentivity at the applied site. However, limited studies exist on novel devices that are superior to those of conventional buccal adhesive systems for the delivery of therapeutic agents through buccal mucosa.

The principle aim of present work is to develop retentive sustained release buccal Diltiazem tablets that avoid hepatic first pass metabolism and mask the bitterness using mucoadhesive agents from natural edible sources. The study mainly focuses on the preparation of the tablets with the best possible combinations of polymers using special punches and evaluation of *in-vitro, ex-vivo* and *in-vivo* parameters. Previous work concentrated on synthetic mucoadhesive materials that are neither biocompatible nor completely biodegradable. Recent researches in this laboratory and similar studies by other workers in different laboratories with natural mucoadhesive materials were found impressive and very encouraging. Since the mucoadhesive agents have been extracted from edible sources they are inherently biocompatible and biodegradable in nature. These substances may be superior substitutes of synthetic polymers.

This thesis is divided into four chapters: chapter 1 describes the fundamentals related to buccal mucosa, principles of mucoadhesion, buccal adhesive drug delivery systems and the monograph of Diltiazem hydrochloride. Chapter 2 describes the methodologies adopted for isolation of mucoadhesive agents, their characterization, formulation of tablets and related studies. Chapter 3 includes the results and discussion of the present investigation. Chapter 4 includes the summary and conclusion, future scope and bibliography.