CHAPTER I

INTRODUCTION

In recent years, the development of intraoral mucoadhesive dosage form has been interested in delivery various drugs via oral mucosa for either local or systemic administration. The intraoral route appears to offer a series of advantages, such as a good accessibility, robustness of epithelium, facile removal of the dosage form in case of need, relatively low enzymatic activity, satisfactory patient acceptance and compliance. Moreover, in the case of systemic delivery, this route offer the advantages of partly circumventing drug degradation in the GI tract and avoiding the hepatic first pass metabolism (Burgalassi, et al., 1996). Eventually, the mucoadhesive dosage forms have replaced a number of conventional dosage forms in medicine and dentistry.

Lidocaine hydrochloride has been a widely used local anesthetic in dentistry since 1948 (Taware, et al., 1997). It blocks the voltage gated sodium channels on excitable membranes, there by preventing the generation and condition of nerve impulses and providing analgesic relief (Comer, et al., 2000). It is usually administered either parenterally or topically. Roller and Ship (1975) designed the study to compare two forms of anesthetic, lidocaine hydrochloride, for oral mucosal biopsies: the traditional injection technique of infiltration with anesthetic solution and a new form of topical application of anesthetic impregnation in a film strip. This study showed that the anesthetic film was easy to administer, producing minimal tissue distortion, and no significant side effects. Most patients liked the film flavoring, and appreciated local anesthesia without needle injection. Brook, et al. (1989) reported that application of lidocaine on the oral mucosa produced soft tissue anesthesia of similar depth and extent to that achieved by infiltration anesthetics. Recently, it was found that topical application of lidocaine to dentine could block the response of the intradental nerves to the probing and air blast stimuli (Amess and Mathews, 1995 and Amess, et al., 1996). One of the main disadvantage of the topical application is the short retention time of the drug on the application site as most of it leaches into the oral cavity shortly after application. The parenteral route of administration is currently the route of choice for the induction of local dental

anesthesia worldwide because of better penetration and rapid onset of action of the drug. This mode of delivery can be painful, especially to pediatric patients. Moreover the increasing risk of acquired immune deficiency syndrome (AIDS) through the use of contaminated syringes has intensified the search alternative to parenteral administration. Mucoadhesive dosage form is potentially to be chosen for the proper choice in pharmaceutical industries.

The mucoadhesive drug delivery systems for oral mucosal administration have been developed in the number of different dosage forms, include films, gels, ointments and tablets (Peh and Wong, 1999). The mucoadhesive films have clearly defined many advantages over other dosage forms. For instance, the films allow more exact dosing and easier application than gels and ointments. In addition, gels were given the relatively short residence time on the mucosa, which is easily washed away and removed by saliva (Kohda, et al., 1997). Although, the mucoadhesive tablets were given the latter advantages too, mucoadhesive films may preferred over adhesive tablet in terms of flexibility and comfort. Therefore, the mucoadhesive films were given more patients' acceptability and patients' compliance than other mucoadhesive dosage forms. The latter advantages are the rationale for developing the mucoadhesive films of lidocaine hydrochloride for oral mucosal administration.

The objective of the present study was to prepare mucoadhesive film for oral mucosal administration of lidocaine hydrochloride as a viable alternative dosage forms to lidocaine hydrochloride injection in dentistry. In this study, the mucoadhesive film containing lidocaine hydrochloride was fabricated by using various mucoadhesive polymers, hydroxypropyl methylcellulose of different grades, Methocel® E4M and E15 and hydroxypropyl cellulose as non-ionic polymers, sodium carboxymethylcellulose as anionic polymer and chitosan as cationic polymer. Since the drug is bitter taste (Michael and Powel, 1986), citric acid and menthol were added in formulation to improve the taste of the obtained films. The prepared films were evaluated for their physicochemical properties. The tensile and bioadhesive properties were also tested. The release of lidocaine form the mucoadhesive film was determined by in vitro method using modified Franz's diffusion cells. And the interactions between ingredients and drug were determined by X-ray diffraction, infrared spectrophotometry and differential scanning calorimetry.