CHAPTER I

INTRODUCTION

Periodontitis is pathological states affecting the gingival, subgingival, periodontal and adjacent tissues (Listgarten, 1986). The primary cause of these diseases is bacteria (Slots, 1979). Most current treatment procedures are directed towards an elimination of the total plaque mass subgingivally as well as supragingivally which include oral hygiene instruction, scaling and root planing (O' Leary, 1986). However, many studies have indicated that antimicrobial therapy can be useful in the treatment of some cases (Genco, 1981) such as pockets over 5 mm (O' Leary, 1986) or bacteria reached the connective tissue (Saglie et al., 1982).

Periodontal therapy has several commonly used antibiotics e.g. penicillins, cephalothin, clindamycin, erythromycin, metronidazole, tetracycline, and minocycline (Genco, 1981). In particular, the tetracycline family of antibiotics has been found to be effective against the microorganisms associated with periodontitis in the gingival crevice. Minocycline is a semisynthetic tetracycline proven to be effective against a broad spectrum of bacteria. Minocycline is the most effective against *Staphylococcus aureus*, particulary those resistant to other tetracyclines (Brogden, Speight, and Avery, 1975). It can inhibit 25 subgingival strains out of 27 (93% inhibition) at 1 μg/mL (Mashimo et al., 1981). It reduces collagen-destructive activity in the gingival crevicular fluid of human periodontal pockets (Golub et al., 1985) and it has an effect on attachment and subsequent of fibroblasts at the root surface (Somerman, 1988).

The use of systemic antibiotics has several disadvantages such as superimposed infections and the high dosage needed to achieve an effective concentration in the gingival crevice (Genco, 1981). This has led researchers to focus on topically applied antibiotics. The use of sustained release delivery systems for local subgingival delivery of antibiotics to the active site of the disease has been studied by several investigators; for example, tetracycline-filled hollow fibers placed in the gingival sulcus were shown to have a dramatic effect both on the periodontal microflora and clinical manifestations of the disease. Furthermore, it was found that drug-filled

cellulose acetate hollow fibers can be manipulated by dental personnel to provide drug therapy with less than 1/1000 of the amount of tetracycline that would have been used for systemic therapy (Goodson, Haffajee, and Socransky, 1979). Films of ethylcellulose containing 30% (w/w) minocycline were prepared as sustained release delivery devices and the results of the short-term clinical study indicated that use of the device in periodontal pockets may cause complete eradication of the pathogenic bacteria from the pocket (Elkayam et al., 1988).

There are several techniques to prepare sustained release dosage form including microencapsulation. Microencapsulation can be described as a process in which very thin coatings of polymeric materials are deposited around particles of solids or droplets of liquids. The microcapsules thus formed range dimensionally from several tenths of a micron to 5,000 microns. Microencapsulation has been used in the pharmaceutical industry for the conversion of liquids to solids, taste-masking of bitter drugs, prolonged or sustained release, separation of incompatibles, reduced gastic irritation, and environmental protection of labile moieties (Bakan, 1986, 1994).

A large number of processes are available for preparing microcapsules, for example, air suspension, coacervation-phase separation, multiorifice-centrifugal, emulsification/solvent evaporation and spray drying (Bakan, 1994). Microencapsulation by emulsification/solvent evaporation is conceptually a simple procedure. It involves the emulsification of a polymer solution containing drug into an immiscible liquid phase containing an emulsifier to form a dispersion of drug-polymer-solvent droplets. The solvent is removed from the dispersed droplets by application of heat, vacuum, or by allowing evaporation at room temperature to leave a suspension of drug-containing polymer microcapsules that can be separated by filtration or centrifugation, washed, and dried (Watts, Davies, and Melia, 1990). Although the emulsification/solvent evaporation technique is a simple procedure, there are many production parameters such as type of polymer, emulsifier concentration and core to wall ratio influencing microparticle characteristics.

The present study was designed to develop sustained release microcapsules of minocycline hydrochloride using the water-in-oil-in-water (w/o/w) solvent evaporation technique because minocycline hydrochloride is a water soluble drug. For drugs with

water solubility, oil-in-oil technique or water-in-oil-in-water technique can be used but one of the drawbacks of using an oil external phase is cleaning-up the final product . The oil has to be removed using organic solvents such as hexane, which themselves may present problems in terms of completeness of removal. However, the problem of removal of oil can be avoided by the use of a water-in-oil-in-water (w/o/w) technique (Watts, Davies, and Melia, 1990). Three biodegradable polymers namely poly (L-lactide), poly (DL-lactide), and poly (DL-lactide-co-glycolide) were selected as a wall material. Biodegradable polymers appear to be advantageous since they can be easily administered and do not have to be removed after the treatment period (Lalla and Chugh, 1990).

The purposes of the study were as follows:

1. To prepare minocycline hydrochloride microcapsules for sustained release by water-in-oil-in-water (w/o/w) solvent evaporation technique by varying polymer type, stabiliser concentration, and core to wall ratio.
2. To characterise the physicochemical properties of minocycline hydrochloride microcapsules, e.g. % yield, morphology, size and size distribution, drug content and drug release.
3. To elucidate the release kinetics of minocycline hydrochloride from minocycline hydrochloride microcapsules.
4. To determine residual dichloromethane content in minocycline hydrochloride microcapsules.