CHAPTER I

INTRODUCTION

Peridontal diseases are a group of conditions, including gingivitis and periodontitis which affect the supporting structures of the teeth. In the development of peridontal diseases, there is an initial of accumulation of plaque at the gingival margin and induction of inflammatory response within tissue and then production of peridontal pocket between the root of the affected teeth and soft tissue. In this protected environment bacteria can accumulate and flourish. If the disease is allowed to progress, increased tooth will loss results. Treatment regimens frequently involve mechanical removal of plaque, usually in conjunction with oral and topical anti-microbial chemotherapy (Soskolone and Freidman, 1996). The clinical efficacy of anti-microbial irrigation solutions is low due to the rapid clearance of the solution by flushing action of crevicular fluid within pocket (Ikinci et al, 2002; Bromberg et al, 2001).

Metronidazole, an effective agent for anti-anaerobic infection, is most frequently used in management of periodontal disease. The long-term use of oral metronidazole in chronic condition like periodontal disease may be associated with certain side effects such as gastro-intestinal disturbances, nausea, anorrexia, vomiting, diarrhea, dry mouth, a furried tongue and glossitis (Genco et al, 1981). However, to avoid the drawbacks of systemic administration, the local action dosage form of metronidazole is desirable in periodontitis. The drug can be given topically into periodontal pocket and can access to site of infection that may be achieved suitable inhibitory concentration of antimicrobial activity with markedly reduced the dose and frequence of drug administration. Furthermore, it reduces the risk of adverse reactions and drug reactions (Seymour and Heasman,1995).

Microemulsion gel and liquid crystal (MEG and LC) offer an interesting and potentially quite promising way for drug delivery system. It composes of four components: oil, water, surfactant and co-surfactant (Attwood, 1994). Although it enjoys advantages of solubility and thermodynamically stable of drug in addition of the target delivery, one of the difficulties in realizing the potential of ME for intra-pocket delivery system is the narrow range of acceptable surfactants and co-surfantants and their high concentration required (Medlicott et al, 1993).

Several approaches have been proposed including the use of the reservoir delivery system (Goodson et al, 1979; Addy et al, 1982), non-degradable polymer system (Friedman and Golomb, 1982), irrigation solutions (Kelly et al, 1985), degradable matrix systems (Britt and Pohlod, 1986; Minabe et al, 1989; Larsen,1990), biodegradable matrix device (Higashi et al, 1990; Steinberg et al, 1991), and biodegradable gel using glycerol mono oleate/sesame oil (Norling et al, 1992).

The requirements for prospective development are the following characteristics; able to be administered by syringes but changing to a viscous semi-

periodontal pocket, slow release of the active substance, biodegradable, good stability with long shelf-life and safety (non-toxic) for oral use (Engstrom, 1992). These characteristics could be obtained from natural or simple pharmaceutical excipient forming to microemulsion gel and liquid crystal instead of lecithin or other gel forming liquid crystal such as glyceryl monooleate (GMO) or other high cost and quality of surfactant product. The method of delivery is particularly useful for the treatment of periodontal disease by insertion of the lamellar gel phase (less viscous and flowable) which is known to absorb water and body fluids in situ and passes directly into the periodontal pocket by using injectable syringes, where water from the gingival fluid induces the spontaneous in-situ formation of the reverse hexagonal or cubic phase structure that has high-viscosity, biodegradability, ability to incorporate and deliver drugs of varying size and water solubility, physical stability (Jaymin et al, 2001).

The high viscosity and stiffness of the hexagonal or cubic phase gel limit the potential use as the delivery system by itself. However, the ability of the less viscous lamellar phase gel to form cubic or hexagonal phase gel upon absorbing more water has resulted in novel drug delivery opportunities in term of routes of administration and applications that can be injected into the periodontal pocket where it would transform into a stiff highly viscous gel and release antibiotic locally preventing infection (Osmond, 2000).

Consequently, the controlled drug delivery in this study could be accomplished by combination with an oil (soybean oil, castor oil and isopropyl myristate); surfactant and co-surfactant (tween 80, cremophor EL, Lutrol F-68, cremophor RH40 and Brij) and water. Upon contact with liquid from gingival fluid the composition may change from lamellar phase gel structure to a reverse hexagonal or cubic phase gel which contacted with the site of action and released the active agent in controlled fashion. These pharmaceutical excipients are accepted to be used in oral and parenteral product (Kibbe, 2000l; Backlund et al, 1999).

Objectives of the study

The aims of this study were following:

1. To prepare and investigate the potential of pharmaceutically acceptable ingredient and to evaluate the appropriate system for metronidazole microemulsion gel and liquid crystal as periodontal drug delivery.

2. To study the physicochemical characteristics of microemulsion gel and to investigate the effect of type and amount of surfactant, cosurfactant and oil on the microemulsion gel system with and without metronidazole.

3. To study the drug release from microemulsion gel and to determine the release kinetics of metronidazole from microemulsion gel system.

4. To study the anti-microbial activity against *P. gingivalis* of investigated metronidazole microemulsion gel and liquid crystal.