CHAPTER I

INTRODUCTION

Vaccines, which can be defined as agents that induce protective immunity against pathogens, have had a significant impact on human health for more than a hundred years. Perhaps, the greatest problem faced in effective delivery of such vaccines is multiple dose 1 immunization regimens are essential. The periodic boosters are required throughout life to maintain immunity. Both in developed and developing countries, a substantial number of infants or childhood fail to receive the number of recommended doses leading to incomplete immunity (Bloom, 1989). Thus, a reduction in number of recommended doses of vaccine not only decreases percentage of partially immunized individuals but also reduces cost. The effort to develop vaccine delivery system by which multidose immunization regimens can be reduced to substantial vaccination or even a single dose has been considerable. One approach to adjuvant design incorporates concepts from controlled-release technology, in which active molecules are delivered from polymeric systems or vesicles at a predetermined rate for a definite period of time. Controlled release systems can be fabricated to deliver vaccine at a constant rate for prolonged periods or to deliver distinct pulses of antigen. Further more, this vaccine delivery system can be localized or targeted delivery of vaccine to antigen presenting cells (APCs) and lymphatic system, prevention of rapid destruction by body of peptide-based vaccine and reduction in number of contacts with recipient. Therefore, controlled release systems offer potential to advance peptide-based vaccines and improve immunization programs by reducing the number of vaccination to a single administration (Aguado, 1993). In recent years, polymeric microparticles have received much attention as vaccine carriers. The polymers used as excipients must meet some

requirements including biodegradable, tissue compatible (no secondary reactions), drug compatible and permeably stable, easy to process, reproducible in formulation and ideally inexpensive (Aguado, 1993).

Many classes of polymers including polyesters, polyamides, polyorthoesters, polyurethanes and polyanhydrides have been used in this system (Hutchinson, 1990). The most widely employs are polyester especially polylactide, polyglycolide and copolymers (Jalil, 1990). These polymers give variation in release period ranging from a few days to well over a year. Furthermore, they have extensive toxicological documentation and consequently approve by the regulatory authorities. Therefore, they are better candidates than other polymers to prepare microparticles for controlled delivery formulations. However, the attempts to use these polymers in microparticle formulation as vaccine delivery systems have been developed for many decades. Some antigens such as Tetanus Toxoid (Alonso, 1994 and Chang, 1996), Staphylococcal Enterotoxin B Toxoid (Eldridge, 1991), HIV-1 vaccine (O'Hagan, 1995 and Cleland, 1996), synthetic malaria antigen (Men, 1996 and Thomasin, 1996), Measles virus (Partidos, 1996), Birth Control Vaccine (Singh, 1995). Human Serum Albumin (Hora, 1990), Rabies virus (Ertl, 1996) and so on were investigated.

Despite the advent of synthetic biodegradable polymers, natural polymers remain much interest because they are natural products, readily available, relatively inexpensive and capable of a multitude of chemical modifications. The natural polysaccharide, chitosan, becomes an attractive polymer with increasing attention as microparticles for controlled delivery systems. It is a biopolymer available in large quantities, excellent in biocompatibility, biodegradability and nontoxicity (Sandford, 1989). However, few studies on the preparation of chitosan microparticles have been carried out. Some active drugs and antigens encapsulated in chitosan microparticles had been reported such as

prednisolone sodium phosphate (Berthold, 1996), ketoprofen (Genta, 1998), aspirin and griseofulvin (Thanoo, 1992), oxantrazole (Hassan, 1992), cisplatin (Wang, 1996), bovine serum albumin (Polk, 1994), tetanus toxoid (Calvo, 1997), diphtheria toxin (McNeela, 2001) and pertussis toxin (Jabbal-Gill, 1998).

Purpose of the study

In this study, Japanese Encephalitis antigen was chosen as a model antigen because it causes a major problem in Thailand. In the present, JE vaccine needs three recommended doses that cause the failure to receive complete immunity.

The objectives of this study are :

1. To encapsulate JE antigen with biodegradable polymers in order to control its release and consequently to prolong its immune response
2. To investigate the effect of process parameters on particle characteristics
3. To determine the degradation of polymers in aqueous medium
4. To elucidate the stability of JE loaded microparticles after exposure to high temperature
5. To evaluate the IgG antibody level from JE loaded microparticles compared to pure JE antigen in animal model

Application of the study

1. To encapsulate JE antigen within microparticles of polylactide, poly (lactide-co-glycolide) and chitosan polymers
2. To prolong release of JE antigen from polymeric microparticles
3. To reduce dose of vaccine administration leading to reduce incomplete immunity
4. To improve stability of JE antigen which encapsulated in polymers
5. To be a conception to develope other single dose vaccines