

CHAPTER I

INTRODUCTION

Streptococcus suis (*S. suis*), one of the principal causative agents of contagious bacterial diseases in pigs, is a gram-positive bacteria facultative anaerobe (David and Blankmore and Stanley, 1994; Higgins and Gottschalk, 2006), rounded-shape with a diameter of 1 micrometer and is observed a single cell, diplococcus or short-chain (Gottschalk et al., 1989). *S. suis* is found in environment particularly in pig herds where both non-pathogenic and pathogenic strains subsist. *S. suis* is a pathogen responsible for a variety of clinical syndromes including meningitis, septicaemia, endocarditis, arthritis, and septic shock in pigs. The severe outbreaks of *S. suis* infection cause high mortality in pigs. *S. suis* is an etiologic agent of streptococcal meningitis in both pigs and human beings (Reams et al., 1994; Gottschalk and Segura, 2000). Especially, *S. suis* type 2 has been recognized as a zoonosis agent (Tarradas et al., 2001; Papatsiros et al., 2011). It poses a risk to human leading to death due to meningitis (Wangkaew et al., 2006; Rasmeechan and Sribusara, 2008).

S. suis strains are identified by various methods such as the presence of specific epitopes on their polysaccharidic capsules. Thirty five different serotypes of capsular polysaccharides have been identified (Types 1 through 34 and ½) (Higgins and Gottschalk, 2006). Serotype 2 is most commonly related with diseases in pigs and human beings, and is the most usually reported serotype worldwide. Virulence is different among various strains of *S. suis*, including muramidase-release protein (MRP), extracellular protein (EP), suilysin (Reams et al., 1994; Gottschalk and Segura, 2000), and adhesions (Higgins et al., 1995; Higgins and Gottschalk, 1999; Wei et al., 2009). The protein can prevent the C₃

complement binding and this process inhibits phagocytosis of white blood cells, and consequently, induces inflammation in meningitis and serositis.

Moreover, the development of effective vaccines is obstructed by the number of virulent serotypes, by the deficiency of knowledge of virulence factors and by difference in virulence among serotypes and within serotypes of *S. suis*. For this reason, the use of antimicrobial drugs is important for the treatment and the controlling of *S. suis* infections in pigs. The prophylactic use of antibacterial drugs has been mixed in animal food and drinking water or injected to the infected animals. However, prior to individual treatment, the in-feed medication must be examined due to efficacy of antibacterial agents, including β -lactams, such as ampicillin, amoxicillin, ceftiofur, cefquinone and penicillin (Schmitt et al., 2001; Plumb, 2005; Papatsiros et al., 2011). Sometime the use of a single antibacterial drug has been unsuccessful in the treatment. Although antibacterial drugs are becoming less effective because of an increase in resistance among *S. suis* isolates and are less accepted because of the public awareness of antibacterial residues, the drugs are still necessary for the treatment. Combinations of antibacterial drugs, such as combinations of cefotaxime and gentamicin, have been used in the treatment of *S. suis* infection in swine farm but there has not been systemically reported about advantages for the use of drug combinations. Thus, it is interesting to study the synergism of combinations of antibacterial drugs for the treatment of *S. suis* infection. Since combinations of β -lactams and fluoroquinolones or aminoglycosides have been widely used in farms, thus these antibacterial drugs are selected to evaluate in this study. Antibacterial agents, prepared as injection dosage forms, are also widely used for the treatment of *S. suis* infected in swine farm. The infected animals are injected once or twice a day for 7 to 10 days. Parenteral suspension dosage form in oil-based medium provides advantages of prolonged release and less hydrolysis reaction. The antibacterial agents, prepared as parenteral suspension dosage form in oil-based medium, are expected to decrease the frequency of drug

administration. Then, the most effective antibacterial agents evaluated in this study will be formulated in the parenteral suspension dosage form.

Therefore, the purposes of this study were to determine the antibacterial susceptibility of local *S. suis* strains, and to formulate antibacterial suspension in oil medium for injection. The synergistic effect of combinations of two antibacterial drugs on those strains was investigated. The effect of components in the formulation, physical appearance, stability, and release of the preparations were investigated.

The objectives of this study were as follow:

1. To evaluate and compare Minimum Inhibitory Concentrations (MICs) of β -lactams, aminoglycosides and fluoroquinolones to local *S. suis* strains collected from Thai swine farms.
2. To study the synergy of combining antibacterial to inhibit *S. suis*.
3. To formulate antibacterial suspensions in oil medium for parenteral administration.
4. To determine physical and chemical stabilities of the preparations and also determine their *in vitro* release.