

CHAPTER I

INTRODUCTION

One of the major health problem in Thailand, and many countries worldwide is infectious disease due to the drug resistant pathogens (Pillay and Zambon,1998; Espinal et al.,2001). Natural products especially medicinal plants have long been prescribed in the traditional medicine for treating various diseases such as infections. Some of these specific medicinal plants and natural products have been found to be active against some specific types of infectious diseases. *Terminalia citrina* ROXB. has been traditionally used in Thailand for treating infectious diseases including diarrhea and skin infections (Burapadaja and Bunchoo, 1995).

Extended spectrum beta-lactamase (ESBL) - producing bacteria are the problem in hospitalized patients and are increasingly associated with community-acquired infections. The emergence of ESBL-producing bacteria are now a worldwide concern. The first isolated in Western Europe in mid 1980s, most commonly in *Klebsiella* spp., followed by *Escherichia coli* with TEM and SHV mutants (Chaudhary and Aggarwal, 2004). In recent years, CTX-M ESBLs have emerged, often in *E. coli*. ESBLs appeared to be increasing among enterobacteria in the periods of 1997 through 2002 (Bouchillon et al., 2002; Nijssen et al., 2004). The prevalence of ESBLs differs from country to country, with the highest percentages in Greece (27.4%) and Portugal (15.5%) and the lowest in the Netherlands and Germany (2.0% and 2.6%, respectively) (Bouchillon et al., 2002). In Thailand, the data from the National Antimicrobial Resistance Surveillance Thailand (NARST) showed the prevalence of ESBL-producing *K. pneumoniae* and *E.coli* in Thailand from 2002 to 2003 were 30.5 % and 19.9%, respectively (Dejsirilert and Apisarnthanarak, 2004). The data from Songklanagarind Hospital reported that 32 % and 19 % of ESBL-producing *K. pneumoniae* and *E.coli* were isolated during the year 2002 (Ingviya and Hortiwakul, 2003).

Cephalosporins and penicillins are the most widely used agents for treatment of severe infections. Unfortunately, extended spectrum beta-lactamases (ESBLs), a heterogeneous group of plasmid-encode enzymes conferring resistance to all penicillins, cephalosporins, and monobactams (Brandford, 2001). Many ESBL-producing organisms are also frequently resistant to aminoglycosides, trimethoprim-sulfamethoxazole, and quinolone.(Rodriguez-Bano et al., 2004). ESBL-producing

E.coli isolates from patients with community-acquired UTI at Songklanagarind Hospital from July 2003 to January 2004 reported that multidrug-resistance patterns and high MIC₉₀ (>256µg/ml) values to ampicillin and high MIC₉₀ (64-256µg/ml) to several antimicrobials including cefazolin, cefuroxime, cefotaxime, gentamicin, and norfloxacin. At present, carbapenems have been considered as the treatment of choice for ESBL-producing pathogens (Burgess et al, 2003; Nathisuwan et al, 2001; Paterson, 2001; Wong-Beringer, 2001; Wong-Beringer et al, 2002) but increased usage has been associated with increase in carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter spp.* (Go et al, 1994; Rahal et al,1998). The use of combination therapy can sometimes result in synergic interaction, thereby, exhibiting antibacterial activity greater than non-carbapenem monotherapy.

Therefore, the purpose of the present study is to determine the susceptibility of ESBL-producing *E.coli* against four antimicrobial agents (ampicillin, amoxicillin/clavulanic, norfloxacin and imipenem) and alcoholic extract of *T. citrina* ROXB. by paper disk diffusion method. The MIC of the two antimicrobial agents (ampicillin and norfloxacin) and alcoholic extract of *T. citrina* ROXB. against all *E.coli* isolates were also determined by the standard agar dilution method. At the same time, the combined antibacterial activities of alcoholic extract of *T. citrina* ROXB. plus ampicillin or plus norfloxacin against norfloxacin resistant- ESBL-producing *E.coli* were also determined by the checkerboard and time kill method. The expected outcome of the study is the information on the antibacterial activities in different aspects of *T. citrina* ROXB. (single and combined with commonly used antibiotics). These will lead to further study in order to determine the active ingredients from plant and the new drug discovery.