

CHAPTER I

INTRODUCTION

Actinomycetes, the filamentous bacteria, have been described as the greatest source of antibiotics since Waksman introduced *Streptomyces* into his systematic screening program for new antibiotics in the early 1940s (Okami and Hotta, 1988). Approximately 71.1% of them could produce the bioactive compounds except for a few of antibiotics that are produced by fungi (18.2%), and a few that are produced by bacteria (10.7%) (Goodfellow, 1988). Organisms belonging to the groups of common actinomycetes, *Streptomyces*, and rare actinomycetes, *Micromonospora*, *Actinoplanes*, *Dactylosporangium*, *Nocardia*, *Actinomadura*, *Microbispora*, *Streptosporangium*, *Kibdelosporangium*, *Kitasatospora*, and others, have been searched for antibiotic production (Oki, 1994).

The best-known genus of actinomycetes is *Streptomyces*, which could produce approximately 80.2% antibiotics, followed by *Micromonospora*, *Nocardia*, and the other genera that could produce about 6%, 3.7% and 10.1%, respectively (Tortora, Funke, and Case, 1995). The data mainly based on the 1976-1986 issues of the Journal of Antibiotics showed that the genus *Streptomyces* yielded many groups of antibiotics such as aminoglycosides, macrolides, ansamacrolides or ansamycin, β -lactam antibiotics, peptides, glycopeptides, anthracyclines, tetracyclines, nucleosides, polyenes, and quinones (Okami and Hotta, 1988).

After the discovery of Penicillin antibiotic by Sir Alexander Fleming in 1929 which led the world to modern remedy, microorganisms have become even more important as the abundant sources of bioactive compounds which are proved to be secondary metabolites. In the discovery of biologically active substances, one important source is microorganisms. Numerous compounds were isolated and showed various biological activities, antibiotic, cytotoxicity, anticholesterol, and anti-inflammatory drug etc. Several of them were developed in pharmaceutical and medicinal use (Goodfellow, 1988).

Red yeast rice, also known as "Red Koji" or "Angkak", obtained as a culture of a fungal species of the genus *Monascus* on rice, has long been used in East Asia as a natural food colorant, e.g. for red rice wine, red soy bean cheese, meat products and fish (Blanc, Loret, Santerre *et al.*, 1994; Ma, Li, Ye *et al.*, 2000; Wild, Toth and Humps, 2002). The genus *Monascus*, belongs to the

class *Ascomycetes* and the family *Monascaceae* (Jůzlová, Martinková and Křen, 1996). This fungus is a source of various secondary metabolites of polyketide structure.

Its use is increasing, especially in western countries, because of the growing interest in natural food supplements. *Monascus* pigments are secondary metabolites possessing an azaphilone skeleton, examples are: orange pigments, e.g. monascorubrin and rubropunctatin, which possess the oxo-lactone ring; red pigments, e.g. monascorubramine and rubropunctamine, the nitrogen analogues of the orange pigments; and yellow pigments such as monascin and ankaflavin (Sato, Goda, Sakamoto *et al.*, 1997). In addition, other non-pigment compounds have also been isolated (Endo, Komagato, Shimada *et al.*, 1986; Hossain, Okuyama, and Yamazaki, 1996; Su, Wang, and Lin, 2003). However, a great number of *Monascus* metabolites have not yet been characterized chemically, and knowledge of their pharmacological and toxicological effects is very limited (Akihisa, Mafume, Ukiya *et al.*, 2004; Hsieh and Tai, 2003; Sabater-Vilar, Maas, and Fink-Gremmels, 1999). Previously, the yellow pigment producing mutants by secondary mutation of a local cassava starch utilizing *Monascus kaoliang* have been screened in our laboratory. One yellow mutant, *M. kaoliang* KB20M10.2, exhibited remarkable yellow pigmentation in submerged culture (Yongsmith, Krairak, and Bavavoda, 1994) as well as in rice solid culture (Yongsmith, Kitprechavanich, Chitradon *et al.*, 2000).

In this study, selected *Streptomyces*, *Kitasatospora* and *Micromonospora* strains isolated from soils were characterized and identified by both classical and molecular techniques. We have chemically explored the secondary metabolite of *Streptomyces* and a yellow mutant of the red yeast rice of *M. kaoliang* KB20M10.2, and herein report the isolation, structural elucidation, and biological activities of the secondary metabolites.

The main objectives of this investigation are as follows

1. To identify and characterize the selected *Streptomyces*, and *Micromonospora* strains from soils of Thailand.
2. To isolate secondary metabolites from the selected *Streptomyces* and *Monascus kaoliang* KB20M10.2
3. To elucidate chemical structures of the isolated secondary metabolites.
4. To evaluate biological activities of the isolated secondary metabolites.