CHAPTER I

INTRODUCTION

Background and problem

Tuberculosis (TB) is major problem of airborne infectious disease in Thailand. People infectioned with *Mycobacterium tuberculosis* (MTB) bacteria in their lungs can transmit the disease to others by coughing. In 2005, 8.8 million people were infected with TB and 1.6 million died. If TB is early diagnosed early and fully treated, people with the disease can quickly become eventually cured, and reduced the risk of transmitting the disease to others.

The rapidly increasing HIV epidemic could also increase the number of HIV-related TB cases. In order to control TB in high HIV settings, the Directly Observed Treatment, Short course (DOTS) strategy should be complemented with additionally collaborative TB/HIV activities. (Public health ministry , 2001)

Drug resistance in tuberculosis is a matter of great concern for TB control programs since there is no cure for some multi-drug resistant TB (MDR-TB) strains of *M. tuberculosis*. There is concern that these strains could spread around the world, and stress the need for additional control measures such as new diagnostic methods, better drugs for treatment, and a more effective vaccine. MDR-TB, defined as resistance to at least rifampicin (RIF) and isoniazid (INH), is a compounding factor for the control of the disease. Since patients harboring MDR strains of *M. tuberculosis* need to enter into alternative treatment regimens involving second-line drugs that is more costly and toxic, and less effective. Moreover, the problem of extensively drug resistant (XDR) strains has recently been introduced. These strains, in addition to being MDR, were initially defined as having resistance to at least three of the six main classes of second-line drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and paraaminosalicylic acid). More recently, at a consultation meeting of the World Health Organization (WHO) Global Task Force on XDR-TB held in Geneva agreed that XDR-TB was TB showing resistance to at least rifampicin and isoniazid, which is the definition of MDR-TB, in addition to any fluoroquinolone, and to at least 1 of the

3 following injectable drugs used in anti-TB treatment: capreomycin, kanamycin and amikacin. XDR-TB now constitutes an emerging threat for the control of the disease and the further spread of drug resistance, especially in HIV-infected patients, as was recently reported. For this reason, rapid detection of drug resistance to both first and second- line.Anti-tuberculosis drugs has become a key component of TB control programs. (Kim TC, Blackman RS, 1984)

According to WHO, in 2007 underdeveloped countries identified TB patient of 14.6 million (90%) and 8.8 million per year of new cases. XDR strains were found in 29 of total 35 countries, mostly in South America and Western Europe. USA spends an average of 10 million bath per patient for treatment.

In 2001, Thailand found treatment registry 58,000 cases. The TB patients were estimated at 91,000 cases, with 13 XDR-TB cases identified. Then rapid diagnosis and identification of drug susceptibility of *M. Tuberculosis* should allow for rapid treatment with a high success rate and reduce the number of active TB and MDR-TB patients. (American Thoracic Society, Centers for Disease Control, 1970)

The laboratory diagnosis of tuberculosis is based on the traditional method of the Ziehl – Neelsen acid fast stain and a laboratory culture. From HIV and MDR-TB problem, we must find a new method used for rapid diagnosis MTB and drug susceptibility. MTT assay is a commercial test for drug resistant with base on culture method. This assay used p-nitrobenzoic acid (PNB) for growth inhibition of MTB, whereas the Nontuberculous mycobacteria (NTM) can growth. We can not only differentiate the MTB from NTM but also rapid detection of drug sensitivity within 7 days. Then this assay can be used for doctor to treat TB patients and reduce MTB spreading to community. (The Department of Microbiology, Faculty of Medicine, Siriraj Hospital, 2006)

Hypothesis

The direct MTT assay can be used for screening drug susceptibility testing and differentiation MTB from NTM as indirect MTT assay.

Objectives

To compare the direct and indirect MTT drug susceptibility testing for *Mycobacterium Tuberculosis* using MTT assay.