

## CHAPTER 1

### INTRODUCTION

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Tuberculosis (TB) is a disease caused by *Mycobacterium tuberculosis*, a pathogenic rod-shaped, active fast bacteria belonging to the *Mycobacteriaceae* family (Narita & Spitters, 2016). According to WHO 2020 data, 10 million people suffer from TB, and 1.2 million people die each year. Indonesia is one of the countries with a high number of TB sufferers. TB infects 845.000 people annually and causes 98.000 deaths, or around 11 deaths per hour ("Kementerian Kesehatan Republik Indonesia", 2021). The Department of Health of the Republic of Indonesia declared in 2021 that the Indonesia's goal is to be TB-free by 2030 (WHO, 2021). TB is classified into two types: active TB and latent TB. Active TB, commonly called TB disease, is when a person starts to develop symptoms. Lee (2016) explains that latent TB occurs when a person is infected with *M. tuberculosis* but has no clinical signs, microbiological evidence, or radiological abnormalities.

To treat active TB, two or more combinations of drugs are used, among which are Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide. However, these drugs may produce side effects such as nephrotoxicity, hypothyroidism, gastrointestinal distress, neurotoxic effects, and ototoxicity. Treatment with only one type of drug should be avoided to reduce the risk of *M. tuberculosis* developing resistance to antibiotics (Jilani et al., 2020; Maiolini et al., 2020).

InhA, also referred to as 2-trans-enoyl-AcpM reductase, is one of the commonly targeted proteins by TB drugs, especially Isoniazid. This is due to InhA's function in *M. tuberculosis* mycolic acid production. Isoniazid must be activated by utilizing katG (catalase peroxidase) to inhibit the binding of InhA and NADH from forming mycolic acid (Shaw et al., 2017). InhA and katG were chosen in this study because they are the standard targets for TB drugs. A mutation in the gene affects katG and InhA proteins, which causes TB to develop resistance to isoniazid.

In Indonesia, *Hibiscus rosa-sinensis*, also known as Bunga sepatu, is common in tropical areas. *Hibiscus rosa-sinensis* belongs to the Hibisceae tribe and family of Malvaceae (Salamah et al., 2018). *Hibiscus rosa-sinensis* flower is known to have antimicrobial effects on gram negative and positive bacteria, as concluded by some studies (Uddin et al., 2010; Mak et al., 2013; Ruban & Gajalakshmi, 2012; Al-Alak et al., 2015). However, a study of this flower's antimicrobial activity with respect to InhA and katG proteins of *M. tuberculosis* through *in silico* methods is unavailable.

In this project, the antibacterial activity of *Hibiscus rosa-sinensis* flower extracts will be assessed using the *in silico* method. The *In-silico* method was chosen to give a vision of the susceptibility of the antibacterial effect of the flower extract using PyRx. Thus, this study aims to assess the antibacterial effect by targeting inha and katG protein of *Mycobacterium tuberculosis* by using *Hibiscus rosa sinensis* flower phytochemicals using *in silico* methods.