

Chapter 1

Introduction

1.1 Background

Antimicrobial resistance (AMR) has been considered one of the most serious global threats to public health. Antibiotic resistance is primarily driven by the overuse of antibiotics to treat bacterial infections, leading to the development of antimicrobial resistance in pathogenic bacteria, rendering current standard antibiotics ineffective (Salam et al., 2023; Tang et al., 2023). Alongside this biological issue, antimicrobial resistance often coincides with inadequate personal sanitation practices in public settings, particularly in dense urban communities, thereby facilitating the rapid transmission of resistant pathogens (Endale et al., 2023). As a result, community-acquired resistant infections are rising. According to data from the World Health Organization (2023), over 1.27 million deaths occurred globally in 2019, resulting in a total of 4.95 million deaths attributable to antimicrobial resistance in pathogenic bacteria. Consequently, antibiotics remain a primary treatment for individuals with bacterial infections. Thus, developing novel compounds or natural alternatives that exhibit powerful antimicrobial activity is crucial as an alternative treatment to combat antimicrobial resistance.

Endophytic microorganisms have recently attracted considerable scientific attention in various studies due to their capability in producing novel bioactive compounds, which may potentially serve as a promising candidate for the development of new therapeutic agents to treat bacterial infections as well as to reduce the rapid rise of antimicrobial-resistant bacterial pathogens (Narayanan & Glick, 2022; Tripathi et al., 2022). Endophytic microorganisms are a group of microorganisms that encompass various bacterial and fungal species that can colonize and thrive within plant tissue, establishing mutualistic relationships with plant hosts in diverse ecosystems (White et al., 2019).

Furthermore, many recent studies have focused on isolating endophytic microorganisms from medicinal plants due to the plants' evidence of exhibiting a high bioactivity profile.

Among these medicinal plant species, *Piper crocatum*, commonly known as the red betel leaf plant, is abundant in Southeast Asia, particularly Indonesia. Notably known for its usage as a traditional medicine to treat oral-related wounds, including toothache and thrush. Furthermore, based on previous evidence, *Piper crocatum* contains diverse phytochemical compounds such as flavonoids, tannins, as well as phenolics that contribute to the plant's bioactivity to be utilized as a part of traditional medicine (K. Assidqi et al., 2022). However, there may be a possibility that there are endophytic microorganisms present has the capacity to synthesize bioactive compounds, amplifying the host plant's medicinal properties. Despite this potential, the molecular evidence regarding these mechanisms remains limited, especially for *Piper crocatum*. Furthermore, current studies neglect the important role of endophytic microorganisms and its biosynthetic capabilities in the plant microbiome, which has resulted in a significant gap in the comprehensive literature.

To address this knowledge gap, this research aims to utilize molecular identification as a robust approach for identifying microorganisms at the taxonomic level. It is highly beneficial for identifying various endophytic microorganism species within the *Piper crocatum* plant. By utilizing short-read or long-read sequencing platforms, such as Oxford Nanopore Technologies, and several bioinformatic tools and reference databases, such as NCBI BLAST and TYGS. Thus, allowing to identify any endophytic microorganisms that may be found and responsible for synthesizing novel bioactive compounds residing within *Piper crocatum*.

1.2 Objective

This study aims to isolate and molecularly identify endophytic bacteria from the leaves of *Piper crocatum* using DNA sequencing, followed by bioinformatic database mining to characterize their biosynthetic gene clusters (BGCs) for secondary metabolite profiles.

1.3 Hypothesis

This study hypothesizes that various endophytic bacterial species within *Piper crocatum* are present and can be identified at a taxonomic level through DNA sequencing. Furthermore, the presence of diverse biosynthetic gene clusters can be found within the isolated endophytes from *Piper crocatum*