Chapter 1

Introduction

1.1 Background

Fungi are widespread organisms found throughout various ecosystems, including marine environments. Despite accounting for 70% of the planet's surface, the marine environment is still biologically unexplored, making it the last frontier of biodiversity (Grossart et al., 2019). Marine fungi are a distinct species that thrive in marine environments, terrestrial or freshwater or coastal waters, and deep-sea environments. Most marine fungi compromise with swimming zoospore-producing groups, yeast, or microfungi (Cunliffe, 2022). Marine fungi comprise approximately 1,900 species across several phyla, with *Ascomycetes* being the most prominent (Jones et al., 2015). The role of marine fungi is crucial for marine ecosystem functioning, including decomposing organic matter from plants, algae, as well as animals and recycled into nutrients; for instance, marine fungi contribute to the calcium carbonate cycle through a process known as endolithic activity and by biodegradation of calcareous substrate (Dievart et al., 2022; Jones et al., 2019). Additionally, marine fungi can form beneficial relationships with other marine organisms by providing essential nutrients or protection against pathogens. The mutualism of marine fungi with other organisms is shown to enhance the health and resilience of their host, such as corals and sponges (Jones et al., 2019; Sen et al., 2022).

The first widely used antibiotic, penicillin, is a natural compound produced by the fungus *Penicillium notatum* and has played a significant role in current antimicrobial treatment, showing fungal natural product significance in medicine (Singh et al., 2019). These initiated the potential novel drug discovery and development of natural compounds from other fungi, including marine fungi. Marine fungi still represent and remain an underexplored group and require further research regarding marine fungi's natural product potential. Moreover, the unique metabolic pathway of marine fungi allows variance secondary metabolites to be synthesized, including polyketides, alkaloids, terpenes,

steroids, polysaccharides, and peptides (Goncalves et al., 2022). These compounds demonstrated promising antibacterial, antiviral, anti-inflammatory, and anticancer activities (Shin, 2020).

The current antiviral, anti-inflammatory, and anticancer face significant limitations that underscore the need for novel therapeutic agents. Antiviral drugs remain inadequate due to narrow-spectrum activity against specific viruses like HIV or hepatitis C, while the rapid evolution of drug-resistant viral strains further, as seen in influenza and SARS-CoV-2 variants (Wang & Li, 2022). Anti-inflammatory therapies rely heavily on NSAIDs, glucocorticoids, and biologics, which often cause severe side effects (e.g., gastrointestinal bleeding, immunosuppression) and fail to address chronic pain effectively (Yang et al., 2024). Lastly, Cancer treatments face challenges with 67% of FDA-approved drugs being authorized based on clinical trials with design limitations, leading to uncertain survival benefits and frequent drug resistance (Hilal et al., 2020). These highlight the urgent need for novel, effective, and accessible therapeutic agents, including those potentially derived from marine fungi, to address these global inequities and treatment limitations.

As the demand for new therapeutics grows in response to the increased incidence of drug resistance and limitation, marine fungi represent a biochemically diverse group of organisms that have become a promising novel bioactive compound source and exhibit promising pharmacological activities for new therapeutic agents, including antiviral, anti-inflammatory, and anticancer therapies. Therefore, further identification of marine fungi's natural bioactive product potential in novel drug discovery was conducted.

1.2 Objective

To isolate, characterize, and assess the bioactivity of marine-derived natural products as a potential therapeutic agent for antiviral, anti-inflammatory, and anticancer treatment through chromatography in silico molecular docking approach.

1.3 Hypothesis

Marine fungi's natural bioactive compound has antiviral, anti-inflammatory, and anti-cancer properties.