Chapter 1

Introduction

1.1 Background

Colorectal adenocarcinoma, a predominant subtype of colorectal cancer (CRC), is constantly becoming a substantial global health burden. Statistics for 2025 indicate that CRC were the fourth most frequently diagnosed malignancy and the third leading cause of cancer-related mortality in Indonesia, with an estimated 80,000 sufferers, with 40,000 new cases and approximately 18,000 fatalities within that year (Lukman, et al., 2024). On a worldwide scale, CRC ranks the top list in both incidence and mortality rates, with a lifetime risk affecting approximately one in 24 men and one in 26 women. Notably, there is a concerning upward trend incidence among younger adults under 50 years of account for roughly 10% of new CRC diagnoses, with an observed increase in cases annually. This epidemiological shift has been associated with lifestyle factors such as sedentary behavior, suboptimal dietary patterns, the including high intake of processed foods and red meat and obesity (Deng, et.al., 2025).

Despite advancements in screening methodologies and therapeutic interventions, the five-year survival rate for patients diagnosed with advanced-stage CRC remains markedly low, emphasizing the limitations of current treatment modalities. The heterogeneity fundamental in CRC and the emergence of resistance to conventional chemotherapeutic and targeted agents contribute greatly to poor clinical outcomes. Besides, molecular complexities, including genetic mutations and oncofetal reprogramming, have been identified as critical factors driving tumor progression and therapeutic resistance, thereby emphasizing the urgent necessity for innovative and efficacious treatment strategies. Although routine screening programs assist early detection, a substantial proportion of patients present with advanced disease stages, where standard treatments comprising surgery, chemotherapy, and targeted therapies exhibit limited effectiveness (Kumar, et al., 2023). The

development of resistance mechanisms during therapy further complicates management, leading to disease recurrence and metastasis, which are primary contributors to mortality. Recent molecular investigations have elucidated detailed pathways involved in carcinogenesis, tumor progression, and drug resistance, emphasizing the unmet need for novel therapeutic approaches that target these molecular aberrations while minimizing toxicity to normal tissues (Wang, et al., 2022 ; Rahadiani et al., 2022).

bajakah, a traditional medicinal plant endemic to the Kalimantan rainforests, has been underexplored in biomedical research but is gaining attention due to its rich phytochemical composition inclusive of flavonoids, alkaloids, tannins, saponins, and phenolic compounds—all of which have demonstrated various biological activities in vitro and in silico investigations (Rustandi et al., 2025). Recent studies have begun to reveal its antioxidant, anti-inflammatory, and cytotoxic effects against many cancer types, including preliminary evidence of efficacy in breast and colon cancer models. Notably, in silico analyses predict that bioactive compounds from bajakah can modulate key cancer-related targets involved in cell proliferation, apoptosis induction (via caspase activation), inhibition of cell migration, and metastasis, aligning with mechanisms distinct from those of cisplatin, which primarily causes DNA crosslinking and damage leading to apoptosis but with broader off-target toxicities (Tejasari, et al., 2022).

One major novelty of bajakah lies in its multitargeted approach mediated by multiple bioactive substances, potentially allowing modulation of diverse signaling pathways such as IGF-1R tyrosine-kinase phosphorylation, apoptotic caspase cascades, and autophagic activity. This contrasts with single-target cytotoxic agents like cisplatin, suggesting bajakah may overcome chemoresistance mechanisms by addressing tumor heterogeneity more effectively. Furthermore, bajakah's antioxidant and anti-inflammatory properties provide an added therapeutic advantage, possibly protecting normal tissues from oxidative damage during treatment (Atun, et al., 2025). However, despite these promising indications, bajakah's use as a standardized anticancer agent remains limited by a lack of

comprehensive in vivo and clinical studies, pharmacokinetic profiling, and formulation standardization.

1.2 Objective

To evaluate the anti-oncogenic potential of bajakah (Spatholobus littoralis Hassk.) extract against human colorectal cancer cells by characterizing its bioactive compounds, assessing its cytotoxic and antioxidant activities, elucidating its molecular mechanisms of action, including inhibition of cell proliferation, induction of apoptosis, and modulation of cancer-related signaling pathways and comparing its anticancer efficacy with cisplatin**.**

1.3 Hypothesis

Bajakah (*Spatholobus littoralis hassk*) extract shows a significant anti oncogenic effects in human colon carcinoma cells by modulating its molecular targets involved in cell proliferation, apoptosis, and metastasis, with greater efficacy and lower cytotoxic effects compared to current chemotherapeutic agents (Cisplatin).