I. INTRODUCTION

1.1 Background

Breast cancer ranks first among cancer cases in Indonesia (IARC, 2022). The breast is an organ composed of epithelial tissue, adipose tissue, and fibrous connective tissue. Histologically, epithelial tissue consists of lobules and ducts, which function in milk production and transportation (Sun *et al*., 2020). Lobules are small functional units responsible for milk production, while ducts are channels connecting lobules to the nipple. Adipose tissue provides shape and cushioning, while fibrous connective tissue supports the breast structure (Siegel *et al*., 2022). Alterations in these epithelial cells can lead to breast cancer, which often begins in the milk ducts and is referred to as ductal carcinoma. A key factor influencing the development of breast cancer is the hormone estrogen (Massardi, 2021).

Estrogen is a steroid hormone crucial in developing and regulating the female reproductive system and secondary sexual characteristics (Yin *et al*., 2020). Additionally, estrogen contributes to maintaining bone health, controlling cholesterol levels, and preserving skin elasticity and vascular tissue integrity. In normal cells, estrogen supports the growth and differentiation of healthy cells, particularly in breast tissue and reproductive organs (Klinge, 2019). However, under conditions of excessive estrogen activity, this hormone can also contribute to breast cancer development by stimulating the growth of estrogen-dependent cancer cells. Estrogen functions in breast cancer by binding to estrogen receptors (ER) in breast cells, subsequently activating signaling pathways that promote cell proliferation and

resistance to apoptosis (Miziak *et al*., 2023). It stimulates epithelial cell proliferation in breast cancer through increased estrogen receptor expression and the induction of estrogen receptor-mediated gene transcription. Estrogen receptors mediate the effects of estrogen and anti-estrogen agents on cells and are predominantly found on the nuclear membrane of target cells (Miziak *et al*., 2023). These receptors are utilized to determine the sensitivity of breast cancer lesions to anti-estrogen therapy and to assess the efficacy of preventive chemotherapy in women at high risk for breast cancer (Rej *et al*., 2024). Estrogen receptors operate by binding to estrogen, which then activates genes that support cancer cell growth. Mutations in estrogen receptors can result in abnormal expression of target cells, predisposing them to malignancy and triggering epithelial cell proliferation in breast cancer (Cunningham *et al*., 2010).

There are two central estrogen receptors involved in breast cancer: estrogen receptor alpha (ER-α) and estrogen receptor beta (ER-β) (Mohtar *et al*., 2021). Both receptors are found in breast tissue and often indicate potentially more aggressive cancer (Ikhtiarudin *et al*., 2022). Activation of estrogen receptor alpha (ER-α) by estrogen triggers gene transcription that supports cancer cell proliferation and survival, making ER-α a primary target in hormonal therapy for breast cancer (Maguire *et al*., 2019). In contrast, estrogen receptor beta (ER-β) can act as a tumor suppressor by inhibiting cell proliferation and promoting cell differentiation (Kim and Kim., 2020).

Additionally, the conversion of hormone precursors into estrogen within breast tissue, facilitated by aromatase, is another critical target in breast cancer treatment. Aromatase is an enzyme that plays a significant role in breast cancer by

converting androgens into estrogen in breast and adipose tissues (Zhao *et al.*, 2020). This estrogen production can influence the growth of estrogen-dependent cancers, particularly estrogen-responsive breast cancer. Elevated levels of aromatase can increase estrogen levels in the body, thereby triggering the onset of breast cancer (Tarannum *et al*., 2019). The activity of estrogen receptor alpha (ER-α), estrogen receptor beta (ER-β), and aromatase can be inhibited by carotenoids (Zhang *et al*., 2012).

Carotenoids are natural pigment compounds that impart yellow, orange, and red colors. They belong to the fat-soluble carotene group and are chemically composed of long chains of carbon and hydrogen atoms (Tanaka *et al*., 2012). Carotenoids exhibit antioxidant properties that are beneficial in inhibiting the activity of the aromatase enzyme, which plays a role in converting androgens into estrogen. Additionally, carotenoids can suppress the elevation of estrogen receptor alpha (ER-α) and estrogen receptor beta (ER-β) levels, which may influence the proliferation of epithelial cells in breast cancer (Zhang *et al*., 2012). The sand lobster (*Panulirus homarus*) is a natural source of carotenoid antioxidants.

Ngginak *et al*. (2017) reported that the types of carotenoids identified in sand lobster (*P. homarus*) include dinoxanthin, diadinoxanthin, zeaxanthin, lutein, astaxanthin, and violaxanthin. Among these, three compounds; lutein, zeaxanthin, and astaxanthin, are known for inhibiting free radicals. However, molecular-level information regarding the activity, interactions, and safety of the carotenoid compounds found in *P. homarus* still needs to be provided. Therefore, this study is essential to provide a foundation for utilizing carotenoid antioxidants from sand

lobster (*P. homarus*) as potential candidates for breast cancer treatment.

1.2 Problem Formulation

The research questions of this study are as follows:

1. How do the interactions and activities of carotenoid compounds found in sand lobster (*P. homarus*) contribute as potential candidates for breast cancer treatment?
2. How safe are the carotenoid compounds found in sand lobster (*P. homarus*) as potential candidates for breast cancer treatment?

1.3 Research Objectives

The objectives of this research are:

1. To perform an in silico analysis of the interactions and activities of carotenoid compounds found in sand lobster (*P. homarus*) as potential candidates for breast cancer treatment.
2. To perform an in silico analysis of the safety of carotenoid compounds found in sand lobster (*P. homarus*) as potential candidates for breast cancer treatment.

1.4 Research Benefits

The benefit of this research is to determine the potential of the sand lobster (*P. homarus*) as an anticancer agent for breast cancer.