Chapter 23
Natural Product Compounds for Breast Cancer Treatment

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ABSTRACT

Breast cancer is the primary cause of cancer death in women. Although current therapies have shown some promise against breast cancer, there is still no effective cure for the majority of patients in the advanced stages of breast cancer. Treatment with present synthetic drugs may lead to a number of adverse effects. Consequently, research into natural product compounds may provide an alternative pathway to determining effective against breast cancer. This chapter reviews molecular targets of breast cancer treatment as well as bioactive compounds sourced from bibliographic information such as Medline, Google Scholar, PubMed databases. The authors hope that this book chapter contributes significantly to previous and ongoing research and encourages further investigation into the potential of natural product compounds in breast cancer.

INTRODUCTION

Cancer is characterized by the uncontrolled presentation of growth and division in the cell cycle, which is mainly caused by a gene mutation in the nucleus of tumor cells. It is a gene events-related sequential progression that can be seen in a single clone of cells. Two cancerous types are malignant and benign tumors. Breast cancer is a malignant type occurring in breast cells and is known as the second cause of cancer-related mortality in both women above 50 years of age and younger women. Age, economic conditions, race, dietary iodine insufficiency as well as high concentration of hormone are the major risk factors associated with breast cancer (Sun, Zhao et al. 2017).

Breast cancer is predominantly induced by inherited mutations of BRCA1 and BRCA2 genes (Filippini and Vega 2013). In addition, the development of breast tumors is also contributed by other factors, including an increase in breast tissue density, obesity, alcohol consumption, physical inactivity and the treatment by hormone therapies such as estrogen, progestin. The pathogenesis of this disease is considered to target two major molecules: estrogen receptor alpha (ERα), a receptor of steroid hormone as well

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as a transcription factor, and epidermal growth factor 2 (*ERBB2*, previously *HER2* or *HER2/neu*) that belongs to family of the epidermal growth factor receptor as a tyrosine kinase-associated transmembrane receptor. In cells of breast cancer tissues, ERα is stimulated by the presence of estrogen, leading to the activation of oncogenic growth pathways. Moreover, ERα signaling is also marked by the expression of steroid hormone-related progesterone receptor (PR). Hence, the fundamental treatment for ER-positive or PR-positive individuals is based on the downregulation of ER signal pathway by using endocrine agents (Mishra, Kumari et al. 2020).

Various treatments are employed for breast cancer management like surgery, radiation therapy, endocrine therapy and chemotherapy. Despite remarkable influences on normal cells, radiations have more effects on damage to cancerous tissues, which exhibit stronger growth, accompanied by the lack of rapid repairable ability. Chemotherapy for patients with cancer is characterized by oral and intravenous administrations of several medicines, however, it also induces severe adverse effects as well as don't use for some breast cancer individuals (Waks and Winer 2019).

Therapeutic agents are employed for breast cancer treatment are including alkylating agent such as cyclophosphamide; anti-metabolite: 5-fluorouracil, methotrexate, capecitabine; hormone and antagonist: tamoxifen, letrozole & anastrozole; miscellaneous: trastuzumab, lapatinib and natural product such as paclitaxel, vinorelbine, doxorubicin. The therapeutic agents used for breast cancer treatment have many adverse drug reactions and these adverse reactions discourage patient adherence to the therapy (Waks and Winer 2019).

In this chapter, we review the up-to-date understanding of natural promising bioactive compounds that present in chemo effective potential against breast cancer. The bioactive compounds have anti-inflammatory, antiangiogenic, antiproliferative, antimetastatic, and anticancer properties. We focus on the possible mechanisms of these bioactive compounds on breast cancer progression.

Curcumin

Curcuma longa Linn., a perennial, tropical herb belongs to the ginger family, is widely cultivated in Asia. Its rhizome is extensively consumed for providing colors and flavors of foods as well as medicinal purposes. Curcumin is commonly used as a natural pigment obtained from the root of *Curcuma longa,* possessing anti-inflammatory, anticarcinogenic, and antimetastatic properties. It was reported that the administration of curcumin resulted in the modifications in the actions and expressions of various important proteins associated with the survival and proliferation of tumors, including enzymes, cytokines, gene-products and transcription factors. Banerjee et al. conducted a study to investigate the significant effects of curcumin on apoptosis, G2/M arrest and decrease in proliferation of cancer cells through assembly dynamics-related inhibition of microtubules as well as activation of mitotic checkpoint in MCF-7 cells (Banerjee, Singh et al. 2010). Another study reported that curcumin had effective ability to induce congregation of cells in the G1 phase, accompanied with zeste homolog 2 (EZH2) down-regulation by activation of three essential enzymes belonging to the mitogen-activated protein kinase (MAPK) pathway, namely p38 kinase, c-Jun NH2-terminal kinase (JNK) and extracellular signal-regulated kinase (ERK) (Hua, Fu et al. 2010). In addition, it was showed that curcumin might be able to affect the association between abnormal expression of signals via the Wnt/β-catenin pathway and breast cancer development by the suppression of slug, β-catenin and cyclin D1 in both MDA-MB-231 and MCF-7 cell lines (Prasad, Rath et al. 2009). Furthermore, prevention of p53 mRNAs, Ki-67 and proliferating cell nuclear antigen (PCNA) expression in breast cancer cells, whereas Bax mRNA expression-related