European Journal of Pharmacology 827 (2018) 125–148

Contents lists available at ScienceDirect

European Journal of Pharmacology

journal homepage: www.elsevier.com/locate/ejphar

Review

Potential phytocompounds for developing breast cancer therapeutics: Nature's healing touch

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ARTICLE INFO

Keywords:
Phytochemical
Breast cancer
In vitro and in vivo
Analogs
Chemotherapy
Limitations

ABSTRACT

Breast cancer (BC) is a devastating disease in female around the world causing significant health care burden in both developed and developing countries. In many cases BC has shown resistance to chemotherapy, radiation and hormonal therapy. Development of new, cost effective, affordable treatment method is the need of hour. Chemical compounds isolated from plants are often biologically active and is attracting the attention of scientific community. Different in vitro and in vivo studies have shown a potential role in reducing the risk of cancer metastasis. Large number of phytochemicals are considered to regulate several molecular and metabolic processes like cell cycle regulation, apoptosis activation, angiogenesis and metastatic suppression that can hinders cancer progression. An extensive review of literature has been conducted to underline the key phytochemicals and their mechanism of action. This review article has discussed in detail the regulatory roles of phytochemicals, their analogs and nanoformulations and the probability of using phytochemicals in therapeutic management of BC. Finally, current limitations, challenges and future perspectives of these phytochemicals are also critically discussed.

1. Introduction

Carcinogenesis is a complex phenomenon which can be classified into three major steps: initiation, promotion and progression. The first step, tumor initiation is a quick process related with exposure of carcinogenic agents to the cells, the distribution of these agents to the cells, the interaction of these agents with DNA resulting in genotoxic effects. The second step, cancer promotion is a prolonged and reversible stage related with proliferation of cancerous cells. The third step, tumor progression is known by tumor cells invasion, growth and metastasis (Steward and Brown, 2013). Based on these three different stages, chemopreventive agents (CPA) have the ability to inhibit, delay or even reverse BC (Amawi et al., 2017). De Flora and his team divided cancer CPA into three main classes. Primary prevention blocks the occurrence of cancer in healthy people by preventing cancer initiation, mutagenesis and promotion. Secondary prevention performs its function directly during the early stages of carcinogenesis, inhibiting tumor progression (i.e., up-regulates antioxidant level, modulate signaling pathways, regulate hormonal and immune status, inhibit angiogenesis). Tertiary prevention is performed through inhibiting invasion and metastasis (i.e., modulate cell-adhesion molecules, inhibit protein degrading enzymes associated with extracellular matrix degradation and activate anti-metastasis genes) (De Flora and Ferguson, 2005; Singh et al., 2016).

1.1. Breast cancer: a global menace

BC is a complex and heterogeneous disease with respect to pathology, biochemistry and is characterized by uncontrolled proliferation of cells caused by the malfunctioning of important genes which are responsible for the synthesis of vital proteins such as anti-apoptotic proteins, tumor suppressers, transcription factors, growth factors and growth factor receptors (Khan et al., 2016; Iqbal et al., 2017). According to United States 2017 BC statistic report, there are around 255180 new cases of BC and 41070 deaths (Siegel et al., 2017). BC is not only restricted to women, but it also has promising effects on men

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https://doi.org/10.1016/j.ejphar.2018.03.007
Received 22 December 2017; Received in revised form 5 March 2018; Accepted 5 March 2018
Available online 10 March 2018

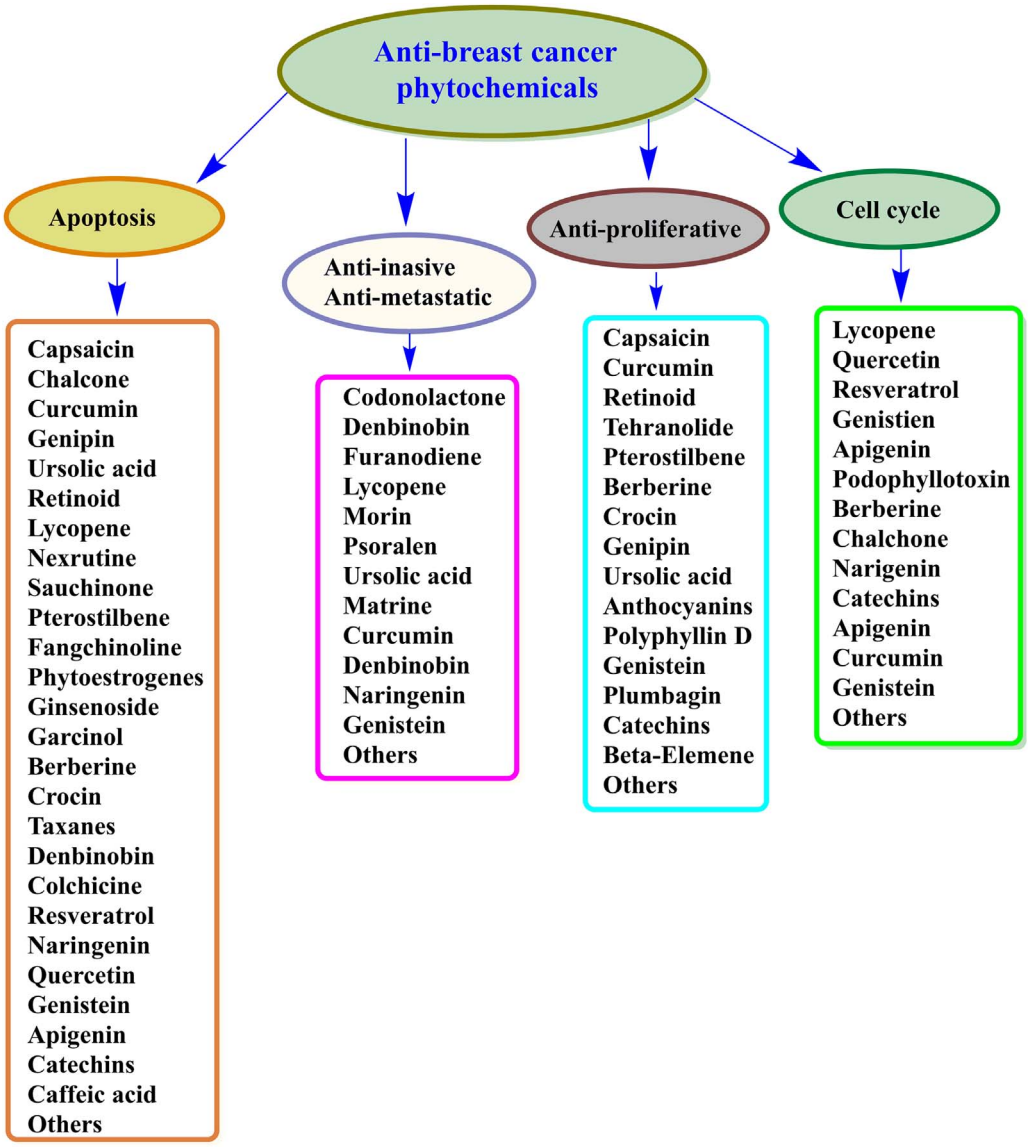

Fig. 1. Chemopreventive effects of natural compounds on breast cancer.

and transgender (Brown, 2015; Grundy et al., 2016).

BC is usually grouped into estrogen receptor positive (ER +) such as, MCF-7 and T47D and ER-negative (e.g., SKBR3, MDA-MB-453, MDA-MB-231 and MDA-MB-468) BC. Based on several other biomarkers such as progesterone receptor (PR), human epidermal growth factor receptor-2 (HER-2), it is further categorized into different other molecular sub-types, such as luminal A (ER + PR + HER2-), luminal B (ER + PR + HER2 +), basal-like and HER2-positive ones (Reis-Filho and Pusztai, 2011; Fedele et al., 2017), phenotypes, basal-like, claudin-low and normal breast-like (Hudis and Gianni, 2011). These distinct subtypes of BC respond differently to treatment which made BC treatment extremely difficult.

There are many factors associated with BC like age, gender, reproductive factors, exo- and endogenous hormonal exposure, weight, previous benign and mammographic density, personal and family history, lifestyle conditions (for example, nulliparity, early menarche, parity, lactation and oral contraceptive use, infectious agents, exposure to known or suspected carcinogens such as tobacco, alcohol consumption, diabetes, obesity, ultraviolet radiation, diet, night work (circadian disruption) and many other substances e.g, asbestos, benzene, radon (Bhatt et al., 2017). The mutation in genetic risk factors such as, BRCA1 and BRCA2 genes is responsible for 5–10% of all BC cases (Li et al., 2017a, 2017b). Several clinical features like age, hormone, HER-2 receptor status, lymph node status, histological grade and presence of metastasis are regularly checked to provide the patient with the best possible treatment (Yersal and Barutca, 2014). The highest incidence rate of BC has been reported in the women of Asian countries due to limited BC health awareness, cultural barriers, timely detection systems, religion, reluctance to visit a male doctor, personal modesty and lack of national diagnosis and screening centers (Naz et al., 2016).

BC is a serious concern and it is very important to speed up its detection, diagnosis and treatment because the earlier we know about the stage of BC, the less the problems will arise. Early stage BC detection can lower down death rates significantly in the future. Because of emerging screening methods, earlier detection schemes and high quality treatment methods has dropped down the death rate to around 20% over the past 10 years (Ng et al., 2017). Scientists have developed several BC diagnostic methods, such as ultrasound, mammogram, ductogram, magnetic resonance imaging, breast self-examination, positron emission tomography, computerized tomography and biopsy etc. But, still these approaches are having some drawbacks such as high cost, time consuming and not appropriate for young female. Development of a highly sensitive and rapid early stage diagnostic methods are the need of hour. Recently, scientists are paying attention to develop