



Review

Are plant-based functional foods better choice against cancer than single phytochemicals? A critical review of current breast cancer research

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ABSTRACT

Breast cancer is the most common malignancy in women worldwide. Over 90% of all breast cancer cases are of different ‘sporadic’ cell types, thus placing emphasis on the need for breast cancer prevention and new effective treatment strategies. In recent years, pre-clinical research provides growing evidence regarding the beneficial action of bioactive plant-derived substances – phytochemicals, on multiple cancer-related biological pathways. The important natural source of various phytochemicals with anti-oncogenic properties are plant-based functional foods. It is hypothesized that a significant anti-tumour activity of plant-based functional foods are the result of a combination of various phytochemicals rather than an isolated agent. The mixture of phytochemicals with various biological activities present in whole foods could have additive or synergistic effects against carcinogenesis. Clinically, it is very important to compare the effect of the isolated phytochemicals against the mixture of phytochemicals present in specific plant-based functional foods. Therefore, the purpose of this review article is to compare anticancer activities of isolated phytochemicals and plant-based functional foods for the prevention and therapy of breast carcinoma. Our conclusion supports the hypothesis that a mixture of wide range of phytochemicals with a plethora of biological activities present in whole plant-derived foods could have additive or synergistic effects against breast cancer. Although, the lack of parallel comparative studies between whole natural foods versus isolated plant compounds limits our conclusion, future pre-clinical and clinical studies evaluating this issue is required.

1. Introduction

Cancer develops over few decades which is characterized by a complex interaction between multiple genes within the cell and its neighbouring tissues, leading to the gradual conversion of healthy cells into cancerous cells [1,2]. Currently, it is initiated by DNA damage as a result of genetic, epigenetic and posttranslational events involved in

carcinogenesis [3]. Less than 10% of all types of cancer are caused by germline mutation, whereas 90% are attributable to somatic mutations, lifestyle factors (including dietary habits), and different types of environmental carcinogens [4,5]. Moreover, current research shows that errors associated with DNA replication also play an important role in the development of cancer [6]. Thus, it appears that the best way to prevent cancer is through rational dietary habits and behaviours, and

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consumption of sufficient amounts of antioxidants and bioactive plant-derived compounds that demonstrate protective effects against carcinogenesis in pre-clinical and clinical studies [7–10].

Excluding non-melanoma skin cancers, breast cancer is the second most common cancer in the world and has remained one of the most frequent cancers among women with an estimated 1.67 million new cancer cases diagnosed in 2012. It is now the fifth cause of death from cancer overall, and the second cause of cancer death in developed regions, and the most frequent cause of death in women in less developed regions [11]. Over 90% of all breast cancers are sporadic in class [12]. Chemoprevention is a potentially effective options for reduction in breast cancer, which has been studied in pre-clinical and clinical oncology in the last thirty years. It is not invasive and appears to be effective, non-toxic, and more economical compared to breast cancer treatment.

The term phytochemicals “are chemical compounds originating from plants” [13]. Evidence indicates that different bioactive phytochemicals can work together with nutrients, vitamins, minerals, and fibre present in whole plant-derived foods, to reduce human diseases. More than ten thousand individual phytochemicals have been identified in plant-derived foods [7,8,14]. Phytochemicals can be classified according to their chemical structure [8,15] (Table 1). Carotenoids, phenolics, and organosulfur compounds are the most studied groups of phytochemicals in experimental and clinical oncology. The terms “nutraceuticals” and “functional foods” are often assimilated with the prevention or treatment of chronic diseases, including cancer. These terms are commonly marketed, but are currently unregulated [16]. Nutraceuticals can be used to describe a food or ingredient of a food whose regular and frequent consumption brings distinct medical and health benefits to individuals [17]. Functional foods has different meanings depending on the country and culture. A latest definition was published by Martirosyan and Singh [18]. Table 2 summarizes characteristics and differences among phytochemicals, nutraceuticals, functional food, and phytopharmaceuticals (dietary supplements).

The mechanism of action of phytochemicals is extensive (briefly summarized in Fig. 1). One specific scientific hypotheses suggests that anticancer activities of plant-derived functional foods result from the combination of phytochemicals, rather than an isolated agent. The mixture of phytochemicals with a range of biological activities present in whole foods could have additive or synergistic effects against carcinogenesis. It is assumed that the isolated plant-derived compound could either lose its bioactivity or may not react the same way as the compound in whole plant-based foods (e.g. its anticancer effect may be much weaker) [8,15]. Oncological research provides growing evidence that regular daily consumption of phytochemicals or whole plant-derived functional foods can lower the risk of breast cancer [19–25].

Table 1
Basic classification of plant-derived phytochemicals (edited by [7–8,14]).

General Categories	Group	Subgroup
Carotenoids		
Phenolics	Phenolic acids	Hydroxybenzoic acids
		Hydroxycinnamic acids
	Flavonoids	Flavonols
		Flavones
		Flavanols
		Flavanones
		Anthocyanidins
		Isoflavonoids
	Stilbenes	
	Coumarins	
Tannins		
Alkaloids		
Nitrogen-containing compounds		
Organosulfur compounds		
Phytosterols		

There are also most recent literature reports reviewing the functional foods and their chemopreventive and therapeutic potential against breast cancer [26–30]. Traditional Chinese medicine (TCM), is medical care system that developed in China over thousands of years, and has been also widely used to control the growth of cancer. Novel natural compounds, single herbs, and combination formulas within TCM could provide therapeutic selectivity against cancer cells and suppress the promotion and progression of cancer without significant off target effects. Thus TCM became an important area of clinical oncology [31]. Within TCM, the anticancer effects of combining various plant compounds to target a range of signalling pathways within cancer cells should be superior compared to single compound targeting only one signalling pathway [31,32–35]. On the other hand, oncological practice showed that any single inhibitor of carcinogenesis would not be sufficient to achieve a sustained anti-cancer response, allowing the growth of multidrug resistance cells [36]. Wang et al. [37] concluded that simultaneously targeting multiple pathways of tumour angiogenesis with a cocktail of natural compounds might be a more effective clinical approach. Moreover, while low-doses of a single compound may not achieve the full anti-angiogenic action, a mixture of compounds, or extracts from medical plants, may be able to specifically synergize in the prevention of carcinogenesis with negligible side effects. This clinical approach could be specifically used for indications such as cancer prevention in high risk individuals or maintenance therapy. Recently, Hussain et al. [38] published a review on the efficacy of whole natural product and isolated constituents against cancer with a focus on prostate cancer. The authors concluded that an overall lack of parallel comparative studies between whole natural foods and isolated phytochemicals limited their conclusions.

1.1. Aim of the study

The purpose of this review article is to compare the anticancer activities of isolated phytochemicals and plant-based functional foods regarding breast carcinoma and to define the role of functional foods in its prevention and therapy. Our hypothesis is that consumption of a mixture of various phytochemicals present in plant-derived functional foods with a wide range of biological activities will have much more health benefits in comparison to single phytochemicals.

1.2. Source of data

Data from the available biomedical literature were reviewed and pooled. Relevant studies published in the English-language literature were retrieved by use of „phytochemicals” or „plant-based functional foods” or „isolated plant compounds” or „synergism” or „fruits” or „vegetables” or „herbs” or „spices” and „anti-tumour activity” or „breast cancer” or „chemoprevention” or „therapy” as either a keyword or MeSH (medical subject heading) term in searches of the PubMed bibliographic database. We focused primarily on the most recent scientific papers from the years 2012–2017.

2. Plant-based functional foods and breast cancer

Anticancer effects of various plant-based functional foods (fruits, vegetables, herbs, spices, and others) were demonstrated in several pre-clinical and clinical breast cancer studies. Some observational epidemiological and clinical studies have confirmed that breast cancer prevalence varies based upon several factors including dietary consumption of plant-derived compounds. Preclinical and clinical studies evaluating the plant-based functional foods for breast cancer prevention and treatment are summarized in Tables 3 and 4.

2.1. Pre-clinical studies - in vitro and in vivo models of breast cancer

Studies using cancer cell lines described several mechanisms of anti-

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