Breast cancer in relationship with dietary antioxidant: possible nutritional and biochemical mechanisms of action: Review study

Yousif Elhassaneen* and Wedad Saif
Department of Nutrition and Food Science, Faculty of Home Economics, Minoufiya University, Shebin El-Kom, Egypt
*Corresponding Author: Yousif12@hotmail.com

Abstract: Cancer is a leading cause of death worldwide. Breast cancer is one of the most common malignancies and contribute significantly to the societal and economic burden of cancer. Racial disparities are evident for breast cancer survival incidence. The reasons for differences in cancer incidence and survival are not entirely clear. However, diet plays an important role in cancer prevention and survival and may also be implicated in racial and ethnic disparities. Diet high in antioxidant content has been associated with reduced breast cancer risk. According to our knowledge, there is a dearth of information regarding the antitumorogenic effects of phytochemicals. Therefore, the present study aims to: investigate the effect of dietary antioxidant of some plant parts including turmeric, marjoram and on breast cancer cells.

Keywords: Antioxidants – Breast cancer cells- phytochemicals.

Antioxidants
Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals. Antioxidants interact with free radicals and may prevent some of the damage free radicals might otherwise cause. An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. Antioxidants terminate these chain reactions by removing free radical intermediates and inhibit other oxidation reactions by being oxidized themselves. As a result, antioxidants are often reducing agents such as thiols, ascorbic acid or polyphenols (Sies, 1997). Antioxidants are also widely used as ingredients in dietary
supplements in the hope of maintaining health and preventing diseases such as cancer and coronary heart disease. Low levels of antioxidants, or inhibition of the antioxidant enzymes, causes oxidative stress and may damage or kill cells (Bjelakovic et al., 2007). The antioxidant hypothesis is strongly sustained to prevent or reduce oxidative damage, their increased uptake from the diet will reduce the risk of chronic diseases. A large part of studies supporting the antioxidant hypothesis against cancer are based on cell lines studies and on animal model where tumors were experimentally induced by high doses of carcinogens (Sporn and Suh, 2002 and Surh, 2003).

**Tested plants as antioxidants**

**Turmeric**

Turmeric (*Curcuma longa*) is an Indian spice derived from the rhizomes of the plant and has a long history of use in Ayurvedic medicine as a treatment for inflammatory conditions (Ammon and Wahl, 1991). Turmeric constituents include the three curcuminoids: curcumin (diferuloylmethane; the primary constituent and the one responsible for its vibrant yellow color), demethoxycurcumin, and bisdemethoxy-curcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins (Negi et al., 1999).

**Effect of turmeric on breast cancer**

Curcumin’s effect on cancer (from an anti-inflammatory perspective (Ireson et al., 2001). Curcumin has exhibited inhibitory effects on several malignant cancers, including breast cancer (Shishodia et al., 2007 and Aggarwal et al., 2007). Curcumin, a phenolic compound extract from rhizome of the plant *Curcuma longa* is found to have inhibitory effects towards a broad range of tumors. In breast cancer, curcumin’s anticancer effect has been anticipated in relating to induce apoptosis at G2 phase of cell cycle via a p53-dependent pathway (Choudhuri et al., 2005). Curcumin, a dietary polyphenol, has been studied extensively as a chemopreventive agent in a variety of cancers, including those of the breast, liver, prostate, hematological, gastrointestinal, and colorectal cancers, and as an inhibitor of metastasis (Kunnumakkara et al., 2008). In a recent report, curcumin was shown to selectively inhibit the growth and self-renewal of breast cancer stem
cells (bCSCs) (Kakarala et al., 2010). The antitumor activity of curcumin in mediating the breast cancer cell proliferative rate and invasion by down-regulating the NF-κB inducing genes. Our findings suggest curcumin could be a potentially therapeutic agent for both ER-positive and ER-negative breast cancer (Rochefort et al., 2003). Recently, our study indicated that turmeric could be exhibited its therapeutic effects in breast cancer through showing strong antioxidant activity because of its high phenolic content 1983 mg GAE. 100 g⁻¹, decreased the human lymphocyte viability, increased the percentage of total damaged spots and decreased in maximal optical density of intact DNA in Ehrlich Ascites Carcinoma cell line. Finally, from the all previous studies, proposed pathways for the effect of turmeric on breast cancer could be shown in Figure (1).

Marjoram

Marjoram (Origanum majorana L., Family: Lamiaceae) is a common spicy medicinal herb, used as a home remedy for the treatment of different ailments. It is a rich source of polyphenols which are known natural antioxidants. Carvacrol and rosmarinic acid have each been reported to protect DNA from a variety of damaging agents and to suppress proliferation of breast cancer cells or cells with active oncogenes. Rosmarinic acid blocked processes associated with breast cancer invasion and metastasis (Jankun et al., 2006 and Karkabounas et al., 2006).

Effect of marjoram on breast cancer

Marjoram used to treat cancers (colon cancer, bancriatic cancer and breast cancer) (Esiyok et al., 2004). Carvacrol and rosmarinic acid have each been reported to protect DNA from a variety of damaging agents and to suppress proliferation of breast cancer cells or cells with active oncogenes. Rosmarinic acid blocked processes associated with breast cancer invasion and metastasis (Jankun et al., 2006 and Karkabounas et al., 2006). O. majorana was shown to possess high activity against cancer in in vitro experiments (Goun et al., 2002). Al-Kalaldeh et al., (2010) detected antiproliferative activity of the ethanol crude extracts of
Figure (1): proposed pathways for the effect of turmeric on breast cancer

Origanum syriacum to MCF-7 human breast adenocarcinoma cell line. Recently, we have shown that *Origanum majorana* suppresses the growth of the triple negative MDA-MB-231 breast cancer cells by causing cell cycle arrest and apoptosis (Al Dhaheri et al., 2013). Recently, our study indicated that marjoram could be exhibited its therapeutic effects in breast cancer through showing strong antioxidant activity because of its high phenolic content (2715 mg GAE.100g⁻¹), decreased the human lymphocyte viability, increased the percentage of total damaged spots and decreased in maximal optical density of intact DNA in Ehrlich Ascites Carcinoma cell line. Finally, from the all previous
studies, proposed pathways for the effect of marjoram on breast cancer could be shown in Figure (2).

**Figure (2):** proposed pathways for the effect of marjoram on breast cancer

**Sweet Violet**

Sweet Violet (*Viola odorata*) is a species of the Family: Violaceae native to Europe and Asia, but has also been introduced to North America and Australasia. It is commonly known as wood violet, sweet violet, English violet (Bruce and Sharon, 2001). *Viola odorata* L. six solvent extract contained the reducing sugar, terpenoids, tannin and
saponins. Volatile oil, salicylic acid methyl ester, saponins, alkaloids. (Ebrahimzadeh et al., 2010). Various phytochemical constitutes (alkaloids, steroids, tannins, flavonoids, and saponins) has been reported in aerial parts of Viola odorata n-hexane, butanolic, methanolic and aqueous extracts (Vishal et al., 2009). The Methanolic extract of the whole plant of Viola betonicifolia has been reported as rich source of alkaloids, flavonoids, tannins, proteins, phenolic compounds, saponins, sterols and triterpenoids (Muhammad et al., 2012).

Effect of turmeric on breast cancer

A liquid extract of fresh leaves used for cancer of the throat and tongue. In other countries, used for breast and lung cancer (Jennings et al., 2001). Viola was investigated for cytotoxicity and reported as pharmacological tools and possibly as leads to antitumor agents in breast cancer (Lindholm et al., 2002).

The aqueous preparations of V. odorata L. Eugenol, Kaempferol, Quercetin, Scopoletin, also show promise in the treatment of many kinds of cancer such as prostate cancer, breast cancer and colon cancer (Marcussen, 2006). Cycloviolacin O2 from Viola odorata is particular promising because of its selective toxicity to cancer cell lines relative to normal cells, which indicates the possibility of its use as an anticancer agent. Analysis of the proposed mechanism of action of this cyclotide shows that the disruption of cell membranes plays a crucial role in the cytotoxicity of cycloviolacin O2 because the damage to cancer cells (human lymphoma) can be morphologically distinguished within a few minutes, indicating necrosis (Svang et al., 2007). Recently, our study indicated that sweet violet could be exhibited its therapeutic effects in breast cancer through showing antioxidant activity because of its high phenolic content (983 mg GAE/100g-1) decreased the human lymphocyte viability, increase the percentage of total damaged spots and decreased in maximal optical density of intact DNA in Ehrlich Ascites Carcinoma cell line. Finally, from the all previous studies, proposed pathways for the effect of sweet violet on breast cancer could be shown in Figure (3).
Figure (2): proposed pathways for the effect of sweet violet on breast cancer

References


علاقة سرطان الثدى بمضادات الأكسدة الغذائية: آليات غذائية وكيميائية: دراسة مرجعية

يوسف عبد العزيز الحساس وداد سيف
قسم التغذية وعلوم الأطعمة - كلية الاقتصاد المنزلي - جامعة المنوفية - شبين الكوم - مصر

يتمثل السرطان أحد الأسباب الرئيسية للوفاة على مستوى العالم. كما يساهم سرطان الثدي وورم الثدي بدرجة كبيرة في الأعباء الاجتماعية والاقتصادية. وحتى هذه اللحظة فما زال الأسباب المتعلقة بأنواع السرطانات المختلفة غير واضحة. ولقد أوضحت العديد من الدراسات أن الوجبات الغذائية بما تحتويه تلعب دورا هاما في الوقاية من السرطان، والتي يرجع غالبا إلى محتواها من المركبات الحيوية المضادة للأكسدة. ونظرا لنقص المعلومات المتعلقة بهذا الجانب فإن الدراسة الحالية تهدف إلى توضيح تأثير بعض مضادات الأكسدة الطبيعية الموجودة بالأجزاء النباتية مثل الكركم، البردوقش، الياسمين الحلو بسرطان الثدي واستيضاح بعض الآليات الغذائية والكيميائية المتعلقة بهذا الخصوص.

الكلمات المفتاحية: مضادات الأكسدة - سرطان الثدي - الكيمياويات النباتية.