The Role of Food–Drug–Cytochrome P450 Interactions in Breast Cancer

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Cytochrome P450 enzymes use a variety of molecules as substrates in enzymatic reactions, mostly catalysing oxidation of these substrates. Some of the enzymes activate carcinogenesis, including breast cancer development. The purpose of the present paper is to review and discuss the interactions between food products and substrates metabolized by enzymes of the cytochrome P450 in relation to the development of breast cancer.
A review of recently published papers was undertaken.
Electronic searches on nutrients, cytochrome P450, and breast cancer were performed on PUBMED, MEDLINE, EMBASE, and EBSCO in March 2018.
Molecular and clinical studies indicate that diet-cytochrome P450 interactions affect the risk for developing breast cancer. However, these are early results which are limited and frequently not reproducible due to possible information bias in food frequency questionnaires. Based on a review of available literature, food products interacting with substrates metabolized by the enzymes of the cytochrome P450 and thus having a direct or indirect effect on breast cancer development were identified.
Nutrition plays an important role in breast carcinogenesis. Eating foods which modify the activity of certain cytochrome P450 enzymes such as CYP1A1, CYP1A2, CYP1B1, CYP2B6, CYP3A4, CYP19A1, and CYP24A1 can contribute to prevention of breast cancer. Diet can act as an adjuvant in the treatment of this disease. Further studies are needed to elucidate the role of nutrients regularly consumed in the development of breast cancer, specifically their effect on substrates metabolized by the cytochrome P450 enzyme family and the corresponding mechanisms.

MeSH Keywords: Breast Neoplasms • Cytochrome P-450 Enzyme System • Food-Drug Interactions • Nutritional Sciences

Full-text PDF: https://www.medscirev.com/abstract/index/idArt/911528

Background

The human cytochrome P450 enzymes (CYP450) catalyze oxidative reactions of a broad spectrum of substrates and play a critical role in the metabolism of xenobiotics, such as drugs and dietary bioactives. Cytochrome P450 first modifies a compound, usually by the addition of oxygen, to make it more polar and hence easier to excrete. This modification can lead to reactive or unstable metabolites that can react further with neighboring proteins or glutathione or rearrange to form new products [1]. In humans, there are 57 genes coding for cytochrome P450 enzymes and more than 59 pseudogenes distributed in 18 families and 43 subfamilies. The most important families for humans are: CYP1, CYP2, CYP3, CYP4, CYP5, CYP6, CYP7, CYP8, CYP11, CYP17, CYP19, CYP20, CYP21, CYP24, CYP26, CYP27, CYP39, CYP46, and CYP51. Numerous drugs are metabolized by these isoenzymes [2].

At present, scientific research on breast cancer is flourishing. The estimated number of new cases of female breast cancer is 124.9 per 100 000 women per year. The survival rate in 5 years is 90%, due to treatment advances in recent years [3].

It is well known that genetics have an important impact on the development and progression of cancer. HER2 (human epidermal growth factor receptor 2) is a growth-promoting protein on the outside of all breast cells**.** Breast cancer cells with higher than normal levels of HER2 are called HER2-positive. These cancers are inheritable and tend to grow and spread faster than other breast cancers [4]. Research evidence supports the idea of a significant interaction between nutrition and genomics, in which diet influences gene expression and metabolic responses. However, the interactions can sometimes have a negative impact on health, increasing susceptibility to diet-dependent diseases. Nutrients affect, among others, the catalytic cycles and metabolic pathways related to the cytochrome P450 enzymes [5].

Cytochrome P450 enzymes use a variety of small and large molecules as substrates in enzymatic reactions, mostly catalysing oxidation of these substrates. Some of the enzymes that activate carcinogenesis are CYP1A1, CYP1A2, CYP1B1, CYP2A6, CYP2B6, CYP2E1, and CYP3A4/5/7 [6,7].

One of the treatments for breast cancer is the modulation of estrogen exposure via ovarian ablation, surgery, irradiation, or medication. Some of the medications available are inhibitors of estrogenic receptors (ER), downregulating ERs or decreasing estrogen production by aromatase inhibitors, such as *Anastrozole* or *Letrozole,* or by selective estrogen receptor modulators (SERM) with tissue-specific activities, such as *Tamoxifen* or *Clomiphene.* Oral chemotherapy is associated with a significant number of medication and food interactions. It is essential that a patient's diet and concurrent medications are thoroughly evaluated by healthcare professionals to provide accurate patient education, therapeutic monitoring, and, if necessary, alternative recommendations, whenever oral chemotherapy is prescribed [8]. The mechanism of action of most drugs that act against breast cancer include the interaction with a CYP450 enzyme, which makes the cytochrome a therapeutic target. The main target in the case of breast cancer is the aromatase enzyme encoded by CYP19, which is responsible for catalysing the biosynthesis of estrogens. The most biologically active estrogen in breast tissue is 17β-estradiol (E2). However, most women develop post-menopausal breast cancer, when plasma levels of E2 have decreased by 90% due to ovarian exhaustion. Thus, the uptake of E2 from the circulation does not appear to contribute significantly to the total content of estrogen in breast tumors. It has been demonstrated that breast tumors and mammary cancer cells possess CYP19A1 necessary for the intra-tumour biosynthesis of estrogens from precursor molecules circulating in the plasma [9]. Thus, the neoplasm induces a local production of aromatase, which increases the effectiveness of aromatase inhibitors in the treatment of breast cancer.

It has been proven that the inhibition of aromatase enzyme reduces estrogen production, thus decreasing the odds for the potential development of hormone-responsive breast cancers [6,10].

The use of complementary medical treatment such as diet and nutritional supplements for women with a previous history of breast cancer is increasingly favored to enhance the action of drugs and reduce their adverse effects.

Moreover, the antioxidant effect of some foods provides an additional benefit. Uncontrolled production of free radicals (radical oxygen-derived species (ROS)) can lead to an increase in mutagenesis in the cells and thus the development of cancer. This production of ROS is mediated by a reaction of oxidation resulting in a variety of inflammatory responses. Normally, cells can defend and protect themselves by producing enzymes such as superoxide dismutase and catalase. In the same way, small molecules such as polyphenols, vitamin C, allopurinol, and uric acid have antioxidant activity. Eating foods with antioxidant properties may have a preventive effect on the development of breast cancer.

Cytochrome P450 mechanism

The cytochrome P450 constitutes a large superfamily of enzymes that catalyse the oxidative transformation of organic substrates (Figure 1). This superfamily of enzymes plays a key role in xenobiotic metabolism and steroid transformation in humans. Activities of the cytochrome P450 enzymes

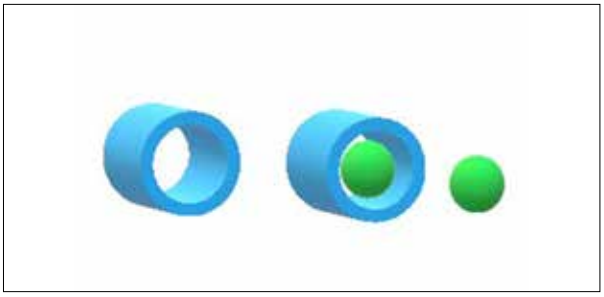

Figure 1. CYP450 (cytochrome P450) with a substrate (S).

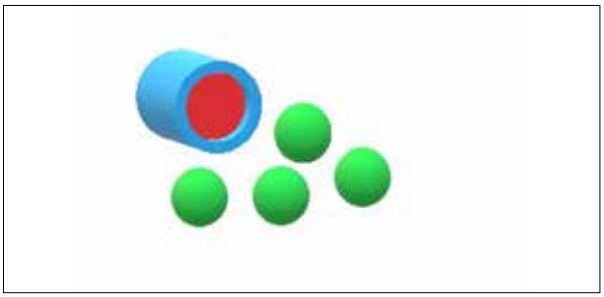

Figure 2. CYP450 with an inhibitor (Inh).

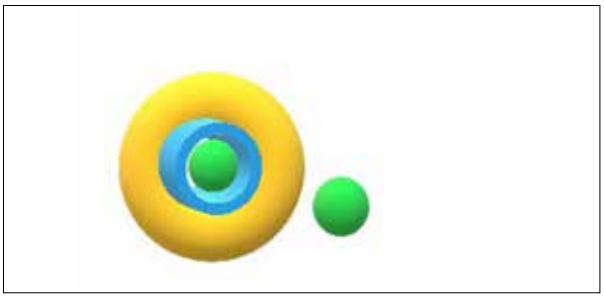

Figure 3. CYP450 with an enhancer (En)

can be affected by diverse genetic and environmental factors that render their metabolism variable. This variability poses a challenge for drug development, which generally targets the inhibition of specific cytochrome P450 enzymes. Inhibition can lead to an increased bioavailability or a decreased elimination of compounds, resulting in a high blood level (Figure 2).

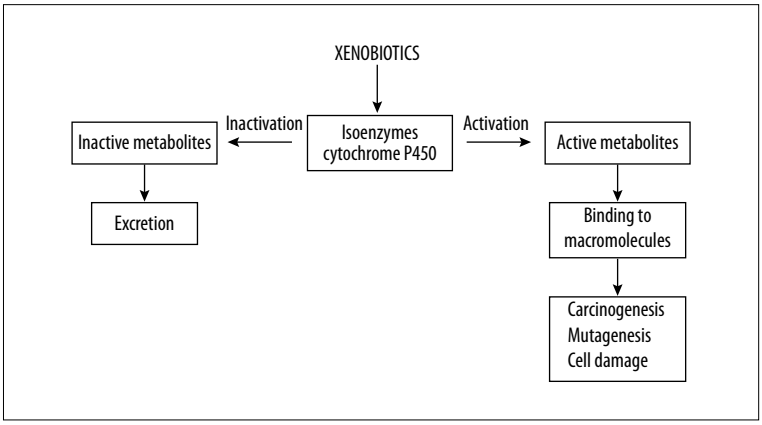

Figure 4. Outline of the mechanisms of CYP450 enzymes [adapted from 23]. An example of activation is the metabolism of codeine to morphine by CYP2D6. Morphine is a very active metabolite. Codeine cannot serve as analgesic medicine in patients who cannot or can only slowly metabolize codeine to morphine. Meanwhile, most of the tricyclics drugs used in mental diseases suffer a process of inactivation and produce inactive metabolites (except for a few substrates such as imipramine, which is metabolized to desipramine (active metabolite)).

However, exogenous compounds can also induce the activity of cytochrome P450 enzymes (Figure 3). In such conditions, the cytochrome P450 enzymes can metabolize a variety of xenobiotics faster (Figure 4) [6,7,11,12].

The aim of the present review was to gather scientific information about how nutrition can interact with substrates metabolized by the enzymes of cytochrome P450, thus modifying its activity and thereby affecting breast cancer development. The clinical applicability of diet as an adjuvant relevant to the treatment of breast cancer is discussed.

Material and Methods

The review strategies, including the search and selection of the articles, are based on guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13].

Sources and research strategy

We performed a literature search using *PubMed*, *EBSCO, EMBASE*, *Medline,* and other sources such as the American Cancer Society and the National Cancer Institute, for articles published in English. The studies were related to the influence of nutrients on cytochrome P450 and how diet can affect the development of breast cancer. The following MeSH terms and research terms were used: "Breast cancer", "Breast cancer and nutrition", "Nutrients and cytochrome P450", "Cytochrome P450 and breast cancer", "nutrition and cancer", "cytochrome P450 substrates", "natural aromatase inhibitors", "Risk factors for breast cancer", "Complementary therapies and breast cancer", and "Nutrition and genomics".

Eligibility criteria

The literature research yielded 2954 bibliographic records only in the first research with "((breast cancer) AND cytochrome

P450)" keywords and 5307 with "(cytochrome P450) AND nutrients". First, duplicates were identified and removed from the pool of bibliographic records. Next, accurate screening of abstracts and titles was performed to determine the most relevant articles. Afterwards, full articles were reviewed using the following inclusion criteria: (1) studies providing information about the relationship between nutrition and breast cancer; (2) studies explaining the metabolic pathways of cytochrome P450 enzymes; (3) studies explaining how some nutrients interact with substrates metabolized by cytochrome P450 enzymes; (4) studies providing clinical information about the pathogenesis of breast cancer; (5) studies providing information about any cytochrome P450 enzyme. In conclusion, 52 studies were retained; these were mostly recent studies, but also included some earlier studies presenting analyses that were not found in the most recent studies.

Results

CYP450 enzymes in breast cancer

Several scientific articles have been analysed to determine which cytochrome P450 enzymes have a significant effect on breast cancer development. It has been shown that cytochrome P450 polymorphisms play an important role in the metabolic activation

Table 1. Food-cytochrome P450 enzymes interactions which influence breast cancer development 0=inhibitor; 1=enhancer; S=substrate

		CYP450 enzymes					
	Food products	CYP1A1	CYP1B1	CYP2B6	CYP3A4	CYP19A1	CYP24A1
Pure substance	Caffeine	–	–	–	S	0	–
	Calcitriol (Vit D)	–	–	–	–	0	0
	Cocoa	0	–	–	–	0	–
	Curcumin	0	–	0	0	–	–
	Dietary lipids	0	0	–	–	–	–
	Ellagitannins	–	–	–	–	0	–
	Estrogens	–	0	–	–	0	–
	Ethanol	–	–	–	–	1	–
	Flavonoids	0	0	–	–	0	–
	Ginseng	–	–	–	0	–	–
	Green tea	–	–	–	–	0	–
	Mangosteen	–	–	–	–	0	–
	Monoterpenes	–	–	–	–	0	–
	Polyphenols	–	–	–	0	0	–
	Resveratrol	–	–	–	0	0	–
	St. John's wort	–	–	–	1	–	–
Spices	Black pepper	0	–	–	0	–	–
	Cardamom	0	–	–	–	–	–
	Cinnamon	0	–	–	0	–	–
	Ginger	0	–	–	0	–	–
	Nutmeg	–	–	–	0	–	–
	Saffron	0	–	–	–	–	–
	White pepper	–	–	–	0	–	–

Table 1 continued. Food-cytochrome P450 enzymes interactions which influence breast cancer development 0=inhibitor; 1=enhancer; S=substrate

		CYP450 enzymes					
	Food products	CYP1A1	CYP1B1	CYP2B6	CYP3A4	CYP19A1	CYP24A1
Vegetables	Broccoli	–	–	–	–	0	–
	Brussel sprouts	–	–	–	–	0	–
	Cauliflower	–	–	–	–	0	–
	Garlic	0	–	–	–	0	–
	Grapefruit	–	–	–	0	0	–
	Grapseed	–	–	–	–	0	–
	Mushrooms	–	–	–	–	0	–
	Onion	0	–	–	–	–	–
	Starfruit	–	–	–	0	–	–
	Soy	–	–	–	–	0	–
	Thistle	–	–	–	0	–	–
	Tomato	–	–	–	0	0	–
Drinks	Beer	–	–	–	0	–	–
	Cabbage juice	–	–	–	–	0	–
	Pomegranate juice	–	–	–	0	–	–
Cereals	Buckwheat	–	–	–	–	0	–
	Millet	–	–	–	–	0	–
	Rice	–	–	–	–	0	–
Meat	Grilled meat	0	0	–	0	–	–
	Smoked meat	0	0	–	0	–	–

of procarcinogens [6,7,11,12]. However, only a few of these enzymes have a direct impact in breast cancer, like CYP1A1, CYP1A2, CYP1B1, CYP2B6, CYP3A4, CYP19A1, and CYP24A1 (Table 1).

Analysis of the influence of nutrients on substrates metabolized by CYP450

As depicted in Table 1, many food products interact with substrates metabolized by cytochrome P450 enzymes, thereby affecting the development of breast cancer. Most of them can be inhibitors, which means they decrease the metabolic function of the cytochrome P450 enzyme they interact with. A few nutrients are enhancers or substrates.

Food products playing an important role in the cytochrome P450 metabolism were classified by category: Pure substances, spices, vegetables, drinks, cereals, and meat.

Pure substances

Caffeine acts as an inhibitor for the CYP19A1 enzyme and as a substrate for CYP3A4 and CYP1A2 [14]. Calcitriol (vitamin D) is an inhibitor of CYP19A1 [12] and CYP24A1 [15]. Also, cocoa is an inhibitor of CYP19A1 and CYP1A1 [16]. Curcumin is a 1A1, 2B6, and 3A4 inhibitor [17]. Dietary lipids are also inhibitors for CYP1A1 and 1B1 [18]. Ellagitannins inhibit CYP19A1 [9]; estrogens are physiological substrates of CYP19A1 and inhibit CYP1B1 [9]; flavonoids inhibit 1A1, 1B1, and 19A1 [47,49]; ginseng inhibits 3A4; and green tea, mangosteen, and monoterpenes inhibit CYP19A1 [9]. Glycyrrhizin acid inhibits CYP1A2, 2B6, and 3A4 and enhances 19A1 [21,22]. Polyphenols and resveratrol inhibit 3A4 and 19A1 [23]. However, ethanol acts as an enhancer of CYP19A1 and St John's wort is an enhancer of CYP3A4 [18,24].

Spices

Black pepper, cinnamon, and ginger are inhibitors of CYP1A1 and CYP3A4. Cardamom and saffron only inhibit CYP1A1, and nutmeg and white pepper only inhibit CYP3A4 [20,26].

Vegetables and fruits

Most of the vegetables listed in Table 1 inhibit CYP19A1, including broccoli, brussels sprouts, cauliflower, grapeseed, mushrooms, and soy, but broccoli and brussels sprouts are enhancers of CYP1A2. Grapefruit and tomato inhibit CYP3A4 in addition to inhibiting CYP19A1. Garlic is also an inhibitor of 1A1 and 19A1. Starfruit and thistle only inhibit CYP3A4, and onion only inhibits CYP1A1 [9,25,26].

As CYP3A4 metabolizes 80% of all substrates, when a nutrient enhances it, the other enzymes involved in carcinogenesis have fewer substrates available. Therefore, enhancing CYP3A4 might prevent carcinogenesis.

Drinks

Drinks such as beer and pomegranate juice inhibit the CYP3A4 enzyme [25,26]. Cabbage juice inhibits the 19A1 enzyme [27–30].

Cereals

Buckwheat, millet, and rice inhibit the CYP19A1 enzyme [9,25,26].

Meat

Some studies reported that grilled and smoked meat can inhibit the CYP1A1, 1B1, and 3A4 enzymes but are enhancers of CYP1A2, which can increase its activity up to 40-fold [31]. The enzymes of CYP1, CYP2, and CYP3 are unspecific, which is why they are influenced differently by nutrients and their effect is difficult to predict.

Influence of polyphenols inhibiting CYP19A1 enzyme

Polyphenols are bioactive chemical compounds present in various foods and beverages and chemically characterized by having 1 or more hydroxyl groups attached to their phenolic groups. Most of the above-mentioned food products are very rich in polyphenols. Numerous studies show that a diet rich in polyphenols, within the framework of balanced nutrition, has numerous beneficial effects on health. Polyphenols play a very important role in decreasing inflammatory processes and oxidative stress. These 2 metabolic processes relate to the incidence of chronic diseases such as diabetes, certain types of cancer, and obesity. The concomitant cellular stress that is generated in these diseases is accompanied by an altered metabolic and inflammatory response in multiple cell types.

One of the isoenzymes on which polyphenols have a significant effect is aromatase (CYP19A1). Table 2 shows the strength with which subgroups of polyphenols inhibit CYP19A1 enzyme [25,26].

Antioxidant capacity of polyphenols and other health benefits

The protective effect of polyphenols is partly due to their high antioxidant capacity. Antioxidants are chemical compounds that promote the elimination from our body of free radicals ROS and waste compounds generated from certain metabolic functions. From a nutritional point of view, an adequate and regular intake of antioxidants is one of the best ways to reduce the relative risk of chronic diseases such as cancer. Some studies suggest that high overall dietary antioxidant capacity is associated with a lower risk of breast cancer [32]. For example, low intake of carotenoids is associated with higher risk of breast cancer among smokers and low intake of flavonoids is associated with breast cancer risk in women over the age of 70 [32]. In addition, an inverse relationship between antioxidant levels and the concentration of plasma C-reactive protein, a molecule that is elevated in the processes that occur with inflammation, has been demonstrated [33–35].

In addition to the antioxidant capacity of polyphenols, it is important to note that substances such as flavonoids, the largest family of polyphenolic compounds, can modulate signal pathways, promoting a whole series of beneficial effects on cells, and thus affecting the different organs and the body as a whole [22,33–36].

Discussion

Several food products affect substrates that are metabolized by cytochrome P450 enzymes. Most of these foods appear to modulate the catalytic activity of a few cytochrome P450 enzymes. The main finding is that natural products can modulate cytochrome P450 enzymes in the same way that drugs do. Some enzymes, such as CYP1, CYP2and CYP3, are unspecific, so they can be influenced differently by nutrients and their effect is difficult to predict. Therefore, nutrition is a very powerful tool to modify cytochrome P450 enzymes and prevent the development of diseases such as breast cancer. Table 1 shows which food products influence metabolism of cytochrome P450 enzymes. Most food products that play an inhibitor role contain polyphenols. Polyphenols can be subdivided into flavonoids (such as tannins, flavones, flavanones, isoflavones,

Table 2. Strength with which different types of polyphenols and biological compounds inhibit aromatase (CYP19A1) [adapted from 23].

Subgroup	Name	Inhibition CYP19A1
Chalcones	Naringenin chalcone	Strong
	Eriodictyol chalcone	Strong
	2,4,2',4'-tetrahydroxy-3' prenylchalcone	Strong
	3'-[y-Hydroxymethyl-(E)-y-methyallyl]-2,4,2',4'-tetrahydroxychalcone 11'-O- coumarate	Strong
	Isogemichalcone C	Moderate
Flavanones	Naringenin	Moderate
	Hydroxyflavanone	Moderate
	7-methoxyflavanone	Moderate
	7-hydroxiflavanone	Strong
	Hesperetin	Strong
	Eriodictyol	Strong
	8-Prentlnaringenin	Strong
Isoflavans	4'-O-Methyglabridin	Weak
	Leiocin	Weak
	Leiocinol	Weak
	Methylequol	Weak
Flavonoids	Chrysin	Strong
	Apigenin	Strong
	Quercetin	moderate
Miscellaneous flavonoids	Coumesterol	Weak
	Rotenone	Strong
Flavones	Flavone	Weak
	7-hydroxyflavone	Strong
	Luteolin	Strong
	7,8-dihydroxyflavone	Strong
	Isolicoflavonol	Strong
	7,4-hydroxiflavone	Strong
	Broussoflavonol F	Moderate
	Methoxyflavone	Moderate
	Rutin	Moderate
Catechins	Epigallocatechin gallate	Weak
	Theaflavin	Strong
	Theaflavin-3,3'-gallate	Strong
	Gallocatechin gallate	Weak

Table 2 continued. Strength with which different types of polyphenols and biological compounds inhibit aromatase (CYP19A1) [adapted from 23].

Subgroup	Name	Inhibition CYP19A1
Lignans	Enterolactone	Moderate
	Norhydroguaiaretic acid	Weak
	4,4'-dihydroxyenterolactone	Moderate
Fatty acids	(10E, 12Z)-9-oco-10,12-octadecadienoic acid	Moderate
	(10E,12Z)-9-hydroxy-10,12-octadecadienoic acid	Weak
	Docosapentaenoic acid	Weak
Peptides	N-benzoyl-L-phenylalanine methyl ester	Weak
Benzenoids	TAN-931	Weak
Sesquiterpene lactone	11BH,13-dihydro-10-epi-8-deoxycumambrin	Strong
	deoxycumambrin	Moderate
Stilbenoid	resveratrol	Strong
	Albanol A	Moderate
Terpenoids	Standishinal	Weak
	Ent-kaurane diterpenoid	Weak
	Aglaiaglabretol B	Moderate
	(–)-dehydrololiolide	Moderate
Xanthones	Mangostin	Strong
	Garcinone	Strong
Anthraquinones	Benzanthraquinone I	Strong

catechins, lignans, stilbenoid, and anthraquinones) and other bioactives not derived from flavonoids. Table 2 shows the strength with which each of these subgroups inhibits the activity of the CYP19A1 enzyme (aromatase) [37].

Aromatase is responsible for a key step in the biosynthesis of estrogens – it transforms androstenedione into estrone and testosterone into estradiol. Estrogens promote the development of some cancers, including breast cancer, so the inhibitors of aromatase are commonly used to treat these diseases [38]. Therefore, to reduce the levels of steroid hormones in the body, aromatase inhibitors could be used to inhibit the reaction. Not all aromatase inhibitors are equally effective, since those with more structural similarity have more affinity to the receptors. Thus, aromatase inhibitor stereochemistry is essential to determine the effect it will have on the development of breast cancer. The quantities used have a large impact on the effect produced. The neoplasm induces local production of aromatase, which increases the effectiveness of aromatase inhibitors in the treatment of breast cancer. When using aromatase inhibitors, estrogen levels decrease in the plasma and locally, mainly in breast "hot spots", decreasing the outbreak or progression of breast cancer. In addition to the pharmacochemical aromatase inhibitors, there are many natural components that can perform the same action, most likely with fewer adverse effects.

Polyphenols, for example, are natural aromatase inhibitors. By simply ingesting products that contain these components, the development of breast cancer could be slowed and even be prevented. They have a double-anticancer action. On the one hand, they induce blockage of the cell cycle of the cancer cells, inducing apoptosis, and on the other hand, they induce the synthesis of detoxification enzymes. Other benefits of polyphenols include cardiovascular prevention, effects on the immune system, and anti-infective effects [23,36]. It is difficult to estimate the quantity of polyphenols needed to prevent breast cancer and which enantiomers have an effect, but it was reported that the tumorigenic potential of cancer cells was significantly diminished at concentrations between 50 and

100 μM of E-resveratrol, and curcumin has been shown to inhibit the formation of breast cancer mammospheres *in vitro* by 50% and 100% using 5-μM and 10-μM concentrations, respectively. Both products are rich in polyphenols [39]. Also, a protein-rich diet including 300 g soy protein corresponds to more than 100 g isoflavones per day helps to prevent breast cancer. Although the potency of isoflavones is a mere per mille of physiological 17β-estradiol, it can significantly modulate estradiol effects at the estradiol receptors due to its high affinity for the alpha receptor subtype, thus inducing a competitive inhibition. They compete for the α-estrogen receptor, and the relative concentrations of estradiol and of isoflavones competing for the receptor determine the long-term prophylactic success [40].

Chronic inflammation contributes to the development of cancer, not only by pro-inflammatory markers, but also by the oxidative stress that it causes. Oxidative stress is the result of an imbalance between the production of reactive species and the activity of antioxidant defence systems. It has been suggested that biologically older woman developed more aggressive breast cancers than their biologically younger counterparts due to the grade of oxidative aging. The amount of reactive species seems to be directly related to the risk of breast cancer [21]. The endogenous and exogenous antioxidant defences protect the cells from the oxidative damage caused by the released radical products, thereby preventing premature cell damage [41]. Food plays a very important role in the appearance of chronic inflammation. Even so, the main mechanism is the local activity of aromatase in breast tissue. Changing nutritional habits can help reduce inflammation and thus reduce the risk of all forms of cancer, diabetes, and other diseases, even if the risk is inherited. Foods that help reduce inflammation include fruits, vegetables, whole grains, and legumes [34,35].

The development of specific nutritional guidelines for breast cancer based on results such as the ones presented in this paper could be a major step forward for diabetes counseling, which could thus contribute to the prevention and therapy of this disease. The main focus is likely to be on prevention and adjuvant pharmacotherapy.

Conclusions

The pathogenesis of breast cancer is complex, but it has been suggested that the metabolic pathway of the cytochrome P450 enzymes plays an important role in the activation and inactivation of pre-carcinogens, along with inter-individual differences and environmental factors. This review article summarizes the findings obtained to date concerning food interactions with substrates metabolized by the cytochrome P450 isoenzymes involved in the development of breast cancer. The presence of reactive species from oxidative stress and inflammation greatly increases the risk of breast cancer. These processes can be targeted with the optimal use of foods with antioxidant and anti-inflammatory capacity. This research field is evolving rapidly and more information will be available in the near future that will help combine drug therapy with dietary counseling to optimize treatment of breast cancer.

Conflicts of interest

None.

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