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PROTECTIVE FACTORS OF NATURAL BIOACTIVE COMPOUNDS: AN INTEGRATIVE REVIEW

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Abstract: Bioactive compounds are nutrients that exert bioactivity in human metabolism, are foods in smaller amounts in the body and have biological properties different from nutritional functions. Currently, several studies have been carried out in order to identify the components responsible for the beneficial properties of foods used in folk and traditional medicine. Thus, the objective of this work was to carry out a narrative review on some of the compounds that have been considered bioactive in foods, evaluating their protective action; presence of organosulfur in Allium sp., fibers, mono and polyunsaturated fatty acids. A search was carried out on the PUBMED, SciELO and Google Scholar platforms considering national and international works published from 2001 to 2021. It was observed that bioactive compounds play an important role in the prevention and treatment of cardiovascular and degenerative diseases such as cancer, diabetes and premature aging. This way, the importance of a diet rich in varieties of fruits and vegetables is highlighted, so that the food is able to offer bioactive compounds in concentrations that are beneficial to the body
Keywords: Antioxidant Micronutrients, Organosulfur, Fatty Acids.

INTRODUCTION

According to Farah and Donangelo (2011), although all nutrients necessary for human metabolism exert bioactivity, they are commonly called bioactive compounds that are minor constituents of foods that have biological properties different from nutritional functions. These compounds, found mainly in plants and in some animals that feed on them, have chemical structures and biological functions that vary widely (GONÇALVES; SILVA; CARLOS, 2019).

In recent years, numerous studies have been carried out to identify the components responsible for the beneficial properties of foods used in folk and traditional medicine. It is known that phenolic compounds and carotenoids have antioxidant activity and can play an important role in the prevention and treatment of degenerative diseases such as cancer, diabetes, cataracts and premature aging (SANTOS et al., 2018). While the organosulfur compounds present in garlic, onion, cruciferous plants and in some herbs have demonstrated anticarcinogenic and cardioprotective properties in experimental models and in clinical studies (CARVALHO et al., 2020). Soluble fibers have been used as adjuvants in reducing plasma cholesterol levels, while insoluble fibers increase the frequency of bowel evacuation and may reduce the risk of intestinal disorders and certain types of cancer (AMORIM et al., 2021).

Although bioactive compounds basically exert extra-nutritional functions, some nutrients such as n-3 series fatty acids and antioxidant micronutrients such as vitamins C and E and selenium are also considered bioactive components in foods, since, in addition to their nutritional function, their metabolism has been linked to beneficial effects at the pharmacological level. The n-3 series fatty acids play an important role in the development of the central nervous system (CNS) and visual acuity (SOUZA; ALMEIDA; LISBOA, 2021). They are important precursors of thromboxanes and prostaglandins, play antithrombotic, antivascular and anti-inflammatory effects (FARAH; DONANGELO, 2011). The anti-inflammatory properties of omega 3 occur by reducing the metabolism of omega 6 and consequent production of pro-inflammatory molecules, since the same group of enzymes are required for the synthesis of pro-inflammatory molecules from omega 6 and anti--inflammatory from omega 3 (AKERELE; CHEEMA, 2016; GOMES et al., 2020).

Considering that there is still a lack of reflection on the protective role of some bioactive compounds, this work proposed to carry out a reflective exercise of the scientific literature on some of the compounds that have been considered bioactive in foods, evaluating their antioxidant action; presence of organosulfur compounds in Allium sp, organosulfur compounds from crucifers, fibers, mono and polyunsaturated fatty acids.

MATERIALS AND METHODS

In order to fulfill the proposed objective, a narrative review was carried out in order to enable an expanded discussion on the topic addressed. This way, the research was carried out from June to July 2021, where the searches were based on the guiding question: Who are and what are the possible protective mechanisms of natural bioactive compounds present in some foods?

The search was carried out in the Pubmed, SciELO and Google Scholar databases, complemented with a manual search in the reference lists of the selected works. The descriptors "antioxidant potential", "functional foods", "bioactive compounds" and "lipid profile" were selected. The searches were carried out considering the following variables: research objective, instruments used, main results and contributions. It is worth mentioning that duplicate articles between the databases were excluded from the study. Thus, original articles, review articles and gray literature in English and Portuguese were included in the study. The selection of articles, national and international official documents covered the period of the last twenty years, 2001 to 2021.

Even though narrative reviews are considered to have less scientific evidence and

are subject to bias due to the random selection of articles (BLAYLOCK; GARDNER, 1994; SCOTT et al., 1999), they are still essential to contribute to the debate of specific themes, suggesting questions and updates on the subject addressed (SCOTT et al., 1999).

Considering the findings related to the research theme, in order to facilitate understanding, the results were divided into five main axes.

RESULTS AND DISCUSSION

ANTIOXIDANT COMPOUNDS

Reactive forms of oxygen and other elements, whose formation is associated with the normal metabolism of aerobic cells, seem to be involved in the induction of different types of cancer. It is known that the consumption of fruits and vegetables rich in antioxidant compounds contribute to the reduction of the risk of cancer, through protection against the accumulation of free radicals (CERQUEIRA; MEDEIROS; AUGUSTO, 2007).

The antioxidants present in fruits, especially phenolic compounds, act as reducing agents of reactive oxygen species (ROS), such as the superoxide radical (O2.-), hydrogen peroxide (H2O2) and the hydroxyl radical (OH.), delaying or preventing the process of lipid peroxidation or oxidation of other molecules, which is why it is important to consume foods that have this characteristic (MITTLER et al., 2011; CAROCHO E FERREIRA, 2013).

In addition to vitamins C, E and selenium, phenolic compounds and carotenoids seem to exert important antioxidant activity in the human body. In addition, compounds such as beta-carotene and lycopene may reduce the risk of prostate, lung, stomach and generalized cancers. Chlorogenic acids (non-flavonoid phenolic compounds) and some carotenoids have been identified as responsible for inhibiting the oxidative stress of cells in culture, exerted by extracts of carrot, Brussels sprouts, burdock, apricot and plum. The main chlorogenic acid, 5-caffeoylquinic acid, was also able to inhibit the induced formation of colon cancer in animals (VIDAL et al., 2012).

Among the phenolic compounds, flavonoids play an important role in relation to antioxidant properties, having been extracted, in recent years, from various plant sources, such as: red grapes (FREIRE et al., 2020), jabuticaba (RODRIGUES et al, 2018), purple passion fruit (MENESES-MARENTES et al., 2019), grape (SILVA et al., 2018; CAMPOS et al., 2017), among others, and can easily be included in the diet of individuals. Anthocyanins, for example, make up the largest group of water-soluble pigments in the plant kingdom, presenting several functions, such as antioxidant action, dyeing capacity, protection of plants against UV radiation, defense mechanism and biological function, among others (KOBUS -CISOWSKA et al., 2020).

Antioxidant compounds can act to prevent cell damage and cancer development in different ways, such as inhibiting the generation of reactive oxygen species, interrupting the propagation of sequential free radical reactions, inhibiting the metabolic activation of carcinogenic compounds and altering the intracellular redox potential. Although the action of antioxidant compounds in reversing cancer in humans has not yet been proven, some studies raise the possibility of using these compounds as correctives and not just preventives. For example, the phenolic compound epigallocatechin-3-gallate, one of the main antioxidants in green tea, was able to induce cancer cells to die in culture, whereas normal cells did not. The caffeic acid phenethyl ester, a phenolic compound found

in bee honeycombs and in propolis, showed this same type of action on cancer cells in culture (VIDAL et al., 2012).

In general, it is recommended that the intake of antioxidants in the diet is quite varied, in order to optimize the possible benefits. There is evidence that, in general, antioxidant compounds act in an integrated manner in the human body, with some of them sparing others, which, in turn, are important for certain vital metabolic reactions in the body (FARAH; DONANGELO, 2011).

ORGANOSULFUR COMPOUNDS IN ALLIUM SP

Allium plants, such as onions, garlic, leeks and chives, are characterized by their strong and penetrating aromas. When the tissue of these foods is damaged, enzymes are decompartmentalized and a series of reactions take place, producing volatile and non-volatile compounds from organosulfur precursors with similar structures between species, but which can produce volatile and non-volatile derivatives with properties sensory and pharmacological differences (OMAR; AL-WABEL, 2010).

Although different pharmacological properties can be attributed to plants of this genus, garlic currently stands out as a functional food due to advances in epidemiological, clinical and biochemical studies that gather evidence about its anticancer activity.

Diallyl thiosulfinate or allicin is a compound formed from the action of the enzyme allinase on the precursor S-(2-propenyl) -I-cysteine sulfoxide. In addition to contributing significantly to the flavor and aroma of garlic, this organosulfur compound has recently received attention for its hepatoprotective effects, by inhibiting cholesterol synthesis, reducing triglyceride and LDL levels, reducing blood pressure, increasing the immunological and anti-atherosclerotic, anti-inflammatory, bactericidal and fungicidal, anti-asthmatic and, mainly, anti-cancer activities (VIDAL et al., 2012). Other sulfur compounds in garlic, such as alliin, allyl sulfide and allyl disulfide, have also been studied, showing bioactivity characteristics similar to those of allicin (RYAN et al., 2009).

The incorporation of selenium in the sulfur compounds of garlic, through the synthesis of new compounds or hydroponics supplemented with selenium, has been studied in order to enhance the anticancer capacity of both food components (GONÇALVES et al., 2015). Non-sulfur compounds that constitute garlic, such as saponins and compounds derived from tetrahydro-beta-carboline, may also contribute to its biological activities, such as the strong antioxidant activity on LDL, and need to be further studied to elucidate the role of garlic in improving cardiovascular health and its other pharmacological effects (CUPPARI, 2002). Heating garlic modifies its pharmacological properties. Some authors suggest that contacting garlic with oxygen in the air before cooking could increase the stability of at least some of its bioactive compounds and, therefore, recommend resting for about 10 minutes after maceration and before cooking. (MARCHIORI, 2003).

Although there are no official recommendations for the intake of garlic's bioactive compounds, the Canadian Ministry of Health and the German Federal Health Agency suggest a daily intake of 4 g of raw garlic or 8 mg of garlic essential oils for the prevention of cardiovascular risk factors, while the American Dietetic Association suggests the consumption of 600-900 mg of garlic per day, an amount equivalent to approximately 1 clove of raw garlic (FARAH; DONANGELO, 2011).

ORGANOSULFUR COMPOUNDS FROM CRUCIFERS

Plants of the Brassicaceae family are commonly called brassicas or crucifers (Cruciferae) due to the great importance of this family in the plant kingdom, since it has about 3,500 species, including food and ornamental species. This family includes all types of cabbage, brussels sprouts, broccoli, cauliflower, watercress, radishes, turnips, arugula, horseradish, black mustard, kale, and kohlrabi. These foods have compounds that are considered to be of great importance for flavor and aroma, due to the pungent sensation they cause and their volatility. Its formation takes place from glucosinolates, by the action of the enzyme myrosinase, after tissue rupture by cutting, during cooking, or during chewing. The products formed from glucosinolates are, in general, isothiocyanates (R-NCS), thiocyanates (R-SCN), nitriles (R-CN) and some volatile compounds (TEIXEIRA; OSELAME, 2013).

In recent years, some of these compounds, mainly isothiocyanates, such as allyl isothiocyanate, have been receiving special attention, not only because of their importance for the flavor and aroma of foods, but also because of their protective action against certain types of cancer in animal models, such as prostate, bladder, digestive organs, breast, lung and kidney (LIU; YANG, 2010; ZHANG, 2010; BHATTACHARYA et al., 2012). Currently, over 100 different glucosinolates have been identified, and they can generate a number of different bioactive organosulfur compounds.

Indole-3- carbinol is another glucosinolate derivative that has received special attention due to its protective action against colon cancer and respiratory papilloma. When in contact with the acidic environment of the stomach, the indole-3-carbinol molecule can combine with other molecules to form condensed products of high anticarcinogenic power. However, the consumption of the compound must be restricted to natural concentrations in food, as there are studies that suggest that in high concentrations it may have a precancerous action, as described for other anticancer compounds (ADWAS et al., 2016).

Some sulfoxides similar to those found in the genus Allium and with the same anti-cancer properties are also found in this family of foods. In cancer prevention, the American Dietetic Association recommends consuming 1/2 cup a day of foods from the cruciferous family (FARAH; DONANGELO, 2011).

FIBERS

In general, it can be said that fibers are polymers present in plant tissues, consisting mainly of carbohydrates, but which may also contain phenolic compounds, glycoproteins and other compounds, arranged in a complex way, in a matrix of amorphous structure, with some tangled cellulose microfibrils. Its composition and structure may differ between plants, between parts of the same plant, and with their stage of maturation, but their participation as a structural cell wall component is a characteristic common to most of them (BERNAUD; RODRIGUES, 2013).

The main physiological characteristic of dietary fibers is that they are, for the most part, neither digested in the gastrointestinal tract nor absorbed intact by humans. Regular dietary fiber intake has been inversely related to a number of diseases such as hypercholesterolemia, obesity, type 2 diabetes, cardiovascular disease, and intestinal disorders and disorders such as diverticulitis, colon cancer, constipation, cholelithiasis, and hemorrhoids (AUNE et al., 2016). However, some authors claim

that the protective effect of fiber against colon-rectal cancer and other diseases may actually come from a dietary pattern that usually accompanies high fiber intake, which includes a high intake of fruits and vegetables, cereals, wholegrain and lean meats and a low intake of red meat, processed meats, sweets and refined grains (FARAH; DONANGELO, 2011).

Dietary fibers can be classified in different ways, and the classification into soluble and insoluble fibers, based on solubility and/or dispersibility in water. Soluble fibers have received special attention in recent years due to their high viscosity. Among them, beta-d-glucan, a linear chain of beta-d-glucopyranosyl units found in oats and barley, stands out in terms of viscosity, although the most abundant soluble fiber in vegetables and fruits is pectin and its derivatives. Legumes, such as peas and psyllium, are also good sources of soluble fiber (BELORIO; GÓMEZ, 2020; LAMOTH et al., 2021).

Viscous fibers have been studied and used as adjuvants in the reduction of blood levels of cholesterol, triglycerides and postprandial glucose. The mechanisms of action do not seem to be fully elucidated, but it is believed that the increase in viscosity in the intestinal lumen may reduce the absorption of these three dietary components, as well as bile constituents produced from cholesterol, by reducing their rate. diffusion through the intestinal wall (BERNAUD; RODRIGUES, 2013). Another proposed mechanism for the decrease in serum cholesterol is that propionic and acetic acids, produced by the fermentation of dietary fibers in the large intestine, could inhibit hepatic cholesterol synthesis (Ladeira et al., 2019).

For the hypocholesterolemic effect of soluble fibers to be observed, they must be consumed in considerable amounts, in association with changes in eating and behavioral habits. For example, a reduction of only 0.3% was observed in plasma levels of cholesterol and triglycerides in subjects whose diets were supplemented for at least 2 weeks with a daily serving of oats, pectin or guar gum. The addition of soluble fiber from oats in 4 meals a day for 7 weeks, accompanied by physical exercises and educational guidance, was able to reduce total cholesterol by 5.6%, LDL cholesterol by 7.1%, LDL cholesterol ratio /HDL in 5.6%, and triglycerides in 14.2% (WANDERS et al., 2011).

It is well accepted that soluble fiber is almost completely fermented by the bacterial flora of the large intestine and therefore plays an important role in its maintenance. Contrary to what used to be thought, a significant part of insoluble dietary fiber is also fermented by the intestinal flora (BROWNAWELL et al., 2012). This happens, for example, in the case of wheat and oat bran, whose insoluble fibers are responsible for about 90% and 80% of their composition, respectively. About 40% of wheat bran and about 70-80% of oat bran are fermented in the large intestine (BOUKID et al., 2018).

Insoluble fiber is, by definition, the fraction of total fiber in food that is not soluble in water or hot buffer. The main components of known insoluble fibers are cellulose, hemicellulose and lignin (MAHAN et al., 2012). The ability of these fibers to retain water and decrease the rate of fermentation in the gastrointestinal tract allows the capture of gases slowly released in the intestine and increases the fecal cake, changing its consistency and stimulating evacuation (STEFE et al., 2008; BROWNAWELL et al., 2008; BROWNAWELL et al. al., 2012).

Water holding capacity can vary greatly between fiber and food types. For example, while the constituent fibers of carrots and lettuce are able to retain water, the fibers of oat

and wheat bran do so much more efficiently. A low-fiber diet can lead to constipation and appendicitis, both in adults and children (SOUSA et al., 2019).

It is well accepted that soluble fiber is almost completely fermented by the bacterial flora of the large intestine and therefore plays an important role in its maintenance. Contrary to popular belief, a significant part of insoluble dietary fiber is also fermented by the intestinal flora. This happens, for example, in the case of wheat and oat bran, whose insoluble fibers are responsible for about 90% and 80% of their composition, respectively. About 40% of wheat bran and about 70-80% of oat bran are fermented in the large intestine (BROWNAWELLAM et al., 2012).

The US Institute of medicine (Medicine Institute of the National Academies) recommends a daily consumption of 38 g of fiber for men aged up to 50 years and 30 g for men over the age of 50 years. For women, the recommendation is 30 g per day until age 50 and 21 g per day after age 50 (FARAH; DONAGELO, 2011).

MONO AND POLYUNSATURATED FATTY ACIDS

Although fatty acids are classified as nutrients because they are essential to human metabolism, some of them have been considered bioactive compounds because they exert an extranutritional function mainly related to reducing the risk of cardiovascular diseases in humans, such as monounsaturated fatty acids (MUFA) and fatty acids. polyunsaturated fatty acids (PUFA).

MUFA have only one unsaturation in their structure. The main MUFA is oleic acid or 9-octadecenoic acid (18: 1 n-9), in which a double bond or desaturation occurs at carbons 9 and 10, by the action of the delta-9-desaturase enzyme, present in both plants as for animals. Some clinical studies associate MUFA consumption with a lower incidence of cardiovascular disease. The replacement of saturated fatty acids by monounsaturated fatty acids seems to be able to promote an increase in serum HDL levels, accompanied by a decrease in LDL and triacylglycerol levels. In addition, LDL become less susceptible to oxidation (SCHERR et al., 2014).

The main source of oleic acid is olive oil. Other sources of monounsaturated fatty acids are peanuts, walnuts, cinnamon and turmeric, and the American Dietetic Association recommends 28-56g of walnuts/day for the purpose of preventing cardiovascular disease (FARAH; DONANGELO, 2011).

The PUFAs are represented by the ω-6 series (the main representatives being linoleic and arachidonic acids) and ω-3 (the main representatives being α-linolenic, eicosapentaenoic [EPA] and docosahexaenoic [DHA] acids). ω-3 and ω-6 are considered essential because they are not synthesized by the body. Linoleic acid (18:2 ω-3) is the precursor of the other polyunsaturated fatty acids of the ω-6 series, whose main food sources are soybean, corn and sunflower vegetable oils. In the ω-3 family, α-linolenic acid (18:3 ω-3) is found in some vegetables, such as canola and flaxseed, and EPA (20:5 ω-3) and DHA (22:6 ω-3) are found in cold and deep water fish (mackerel, sardines, salmon, herring) (BORGES et al., 2014).

The US Institute of medicine, considering a total lipid percentage of 20-35% of energy intake in adults, recommends that n-6 fatty acids (primarily linoleic acid) account for 5-10% of energy intake and that n-3 (mainly alpha-linolenic acid) are responsible for 0.6-1.2%. This proportion is also recommended for children and adolescents, although these groups tend to ingest more lipids than adults (FARAH; DONANGELO, 2011).

During pregnancy and lactation, the use of diets enriched with omega 3 was associated with reduced adiposity, decreased adipocyte size and decreased serum leptin levels (SARDINHA et al., 2013).

Maternal consumption of docosahexaenoic acid (DHA; 22:6) through fish and/or fish oil supplementation has an important role in the development of the central nervous system, in high-risk pregnancy, in the increase in birth weight, length and head circumference, visual acuity, hand-eye coordination, attention, problem solving and information processing, immunity and autonomic nervous system response (ALMEIDA et al., 2014).

PUFA fatty acids through their binding to PPARs (peroxisome proliferator-activated receptor) can regulate lipid metabolism, acting to improve the expression of genes related to fatty acid oxidation (KHAIRE; KALE; JOSHI, 2015). It has also been shown that the intake of omega-3 is capable of playing a dose-dependent hypotensive role in hypertensive individuals, mainly due to its anti-inflammatory action by decreasing the synthesis of arachidonic acid derivatives: prostaglandin E2, thromboxane A2, prostacyclin and leukotriene B4 (SANTOS et al., 2013). It is verified that omega-3 and its derivatives EPA and DHA can act as cytoprotectors, through the positive regulation of antioxidant enzymes and inhibition of pro-inflammatory gene expression (DOSSI et al., 2014).

FINAL CONSIDERATIONS

The present study sought to synthesize the knowledge related to the application of bioactive compounds in the practice of clinical nutrition in order to recognize, mainly, their antioxidant and anti-inflammatory potential. The importance of a diet rich in varieties of fruits and vegetables, whole grains, legumes, roots, oilseeds, fermented dairy products, oils rich in monounsaturated fatty acids and in the n-3 series is highlighted, so that the food is able to provide the individual with a supply of bioactive compounds sufficient to improve health. In addition, bioactive compounds are efficient in improving pathological conditions such as cancer, diabetes and cardiovascular diseases, so the intake of these compounds in the diet is important in the quality of human life.

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