Nutraceuticals: the Link Between Lifestyle and Medicine
A review

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Abstract
Numerous studies have reported positive associations between certain biologically active compounds, with pharmacological properties, such as nutraceuticals, contained in some foods and various pathologies. The term "nutraceutical" currently varies from country to country, referring to a number of valuable molecules, derived from organic sources (plants) or foods such as polyphenols, essential amino acids, antioxidants, soluble fiber, polyunsaturated fatty acids (PUFA), prebiotics, prebiotics, which act at the cellular level, in combating oxidative stress and inflammatory processes and / or in altering the expression of some genes. The discovery of the many benefits attributed to these products and the ever-changing lifestyle have contributed to increasing consumer confidence in nutraceutical and functional foods around the world, and there is a growing interest in improving the quality of life and adopting a healthy lifestyle. to prevent or reduce the risk of disease. Based on these considerations, this paper aims to review some scientific evidence obtained from in vitro / in vivo studies, which supports the beneficial effects of some nutraceuticals and their medical implications in various pathologies.

Keywords: nutraceuticals, bioactive compounds, therapeutic effect, pathologies

1. Introduction

In recent years, increasing the body's endurance and prolonging its life have become major priorities for relevant fora around the world. The interest of companies in food quality and how it influences the evolution of life, but also in the development of modern technologies, such as immobilization, nanotechnology and / or encapsulation, to obtain compounds such as nutraceuticals, the top priority property for both food, as well as for the pharmaceutical [1-3].
ENA (European Association of Nutraceuticals) [2016], makes a clear distinction between nutrition / food and medicines or pharmaceuticals. According to ENA, food provides nutrition in the form of substances necessary for the normal development and maintenance of human body functions, while medicines are always preferred as a therapeutic aid in terms of health and treatment of various actions ENA [1].
The term *nutraceutical* results from the combination of two words, "nutrient" (a nutritious food component) and "pharmaceutical" (a medicinal product), referring to any biologically active substance or substance isolated from the matrix of a food, in a concentrated form, perfectly compatible with the human body and which supports in a positive way its physiological and metabolic functions, but which is not recommended to be consumed as a food to replace meals or diet [4-6].

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Although many benefits of these products have been discovered, due to their mechanisms of action, such as antioxidant and anti-inflammatory activity, there are still a number of key issues, such as bioavailability, degree of metabolism or dose used, which are not yet fully understood. known and which raises a number of legislative issues regarding the regulation of their use on the market [7-10]. Based on these considerations, the aim of this study is to present some of the main classes of substances with nutraceutical effect and to reproduce some of their medical benefits, in adopting a healthy lifestyle, which prevents or reduces the risk of occurrence of diseases.

2. History

The relationship between food and medicine has been traced back to antiquity in countries such as Greece and China, and sends us back in time, 3,000 years ago, to the time of the "father of medicine," Hippocrates, who said "let your medicine be food and your medicine be your food ", a concept preserved to this day. In the early 1900's, the scientific interest in the connection between food and medicine grew rapidly, in countries such as the United States and Japan. In the mid-1980s, health authorities launched the concept of "functional food", referring to those products which, in addition to the basic nutritional principles, contain active substances with beneficial effects on health. The idea of designing these products was born from the desire to improve the quality of life, to adopt a healthy lifestyle and to be able to prevent or reduce the risk of disease [6, 11].

In 1989, Stephen DeFelice, founder and president of the Foundation for Medical Innovation in Cranford, New Jersey, first coined the term "nutraceutical." According to him, a nutraceutical can be said to be "a food or part of a food, which provides medical benefits, in the prevention and / or treatment of a disease".

Audrey, M., et al., [2004] state that nutraceuticals are biologically active ingredients, present in functional or separate foods and that have physiological benefits on human health, intervening in altering cellular metabolism and protection against serious diseases [12]. Subsequently, in countries such as England and Japan, nutraceuticals become an integral part of the food landscape, and diet is beginning to be considered for the first time in Germany, France and the United Kingdom a more important factor in maintaining health than exercise or hereditary factors [6]. In India, nutraceuticals are considered as food components, obtained from plant raw materials or botanical plants, which are used to prevent or treat various types of chronic and acute diseases [13].

3. Nutraceutical classes

A number of "in vitro" scientific studies support the biological activity of nutraceuticals, but human clinical trials are few and far between. Sometimes this term has a broader meaning similar to all products with special pro-health properties and includes any biologically active substance or substance used as part of a food that positively alters the body's physiological and metabolic functions, such as nutrients and biologically active phytochemicals, food supplements, functional foods and herbal products, as well as genetically engineered beverages and foods, presented in the form of tablets, capsules, powders, liquid preparations, individual supplements or in various combinations [3, 5, 14-16].

The definition of the term "nutracetic" differs greatly from country to country, and their classification generally depends on their origin, their chemical composition, their mechanism of action, but also their pharmacological conditions.

Ciepłucha, K. [2004], Prabu, L.S. et al., [2012], Bagchi, D. and Nair, S., [2016], Santini, A. et al., [2018] consider that, depending on their origin, nutraceuticals may be of plant, animal and microbial origin [17-20] (Table 1).

Table 1. Classification of nutraceuticals by their origin

Nutraceuticals of plant origin		Nutraceuticals of animal origin	Nutraceuticals of microbial origin
Allicin	Isoflavone	Coline	*Bifidobacterium bifidum*
Ascorbic acid	Lignin	Coenzyme Q10	*Bifidobacterium longum*
tocopherol	Luteolin	Conjugated linoleic acid - CLA	*Bifidobacterium infantis*
ß -carotene	Lutein	Creatine	*Lactobacillus acidophilus*
ß-glucan	Lycopene	Lecithin	*Saccharomyces boulardii*
Capsaicin	Minerals	Minerals	*Streptococcus salvarius* (*subs. Thermophilus*)
Cellulose	Pectin	Sphinolipids	
Daidzeine	Phenolic acids		
Fatty acids	Phytic acid		
Gallic acid	Phytosterols		
Genistein	Saponins		
Geraniol	Sterile alcohol		
	Quercetin		
	Zeaxanthi		

It has been found that the most widely used nutraceuticals are compounds derived from plants, fruits, vegetables, colostrum or bee products and often have important antioxidant or anti-inflammatory properties, which provide protection against chronic diseases such as cardiovascular disease, diabetes, cancer or osteoporosis [14, 21-23].

Chauhan, B. et al. [2013] divided the substances with nutraceutical effect into:

- nutrients, substances with well-established biological functions: vitamins, minerals, amino acids and fatty acids;
- phytochemicals, herbal compounds;
- compounds derived from other sources: dietary supplements, supplements used in sportsmen nutrition and weight loss supplements [24] (Figure 1).

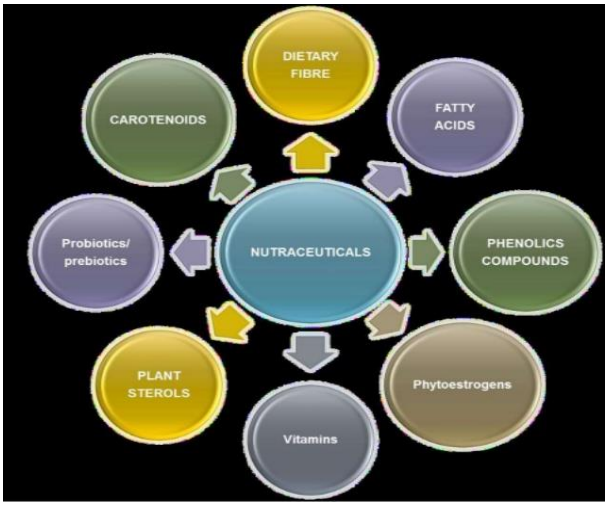

Figure 1. Classification of nutraceuticals [24]

According to their chemical nature, the most important classes of nutraceuticals are considered terpenes and their derivatives (carotenoids, saponines, tocotrienols, tocopherols), polyphenolic compounds (coumarin, tannins, lignin, anthocyanins, isoflavones, flavones, resveratrol), fatty acids and their isomers (PTS, PEP, CLA, JKT, lecithin, sphingolipids), carbohydrates (ascorbic acid, oligosaccharides), proteins and amino acids (allylic compounds, folic acid, isothiocyanin, choline, indoles), minerals (Ca, Se, K, Cu, Zn) and some microorganisms (probiotics, prebiotics) [18, 20, 22].

According to the source, the nutraceuticals were divided into two classes:

- natural (traditional) nutraceuticals, naturally contained in various food sources: chemical constituents, nutraceutical enzymes and probiotic microorganisms;
- non-traditional nutraceuticals, represented by products obtained through different biotechnological processes: fortifying foods and recombinant products.

4. Therapeutic implications

Numerous studies have highlighted remarkable results of nutraceutical compounds in various pathologies such as Alzheimer's disease (AD), diabetes, atherosclerosis, cardiovascular disease, cancer, neurological disorders, kidney or gastrointestinal disorders.

Prevention and treatment of high blood pressure and cardiovascular disease

Cardiovascular disease is the leading cause of death worldwide, with 45% of heart attacks and 51% of strokes resulting in more than 9.4 million deaths worldwide each year [25].

Experimental studies have shown that, although their etiology was multifactorial, the consumption of foods with a high content of nutraceuticals in the form of vitamins, minerals, polyphenols, flavonoids, dietary fiber and omega-3 polyunsaturated fatty acids (n-3 PUFA), associated with lifestyle change and exercise use improve endothelial function in heart transplant patients and heart risk, decrease the incidence of myocardial infarction and angina pectoris [26, 27].

Polyphenols and flavonoids are the most abundant secondary metabolites in the plant kingdom [28], naturally present in fruits, vegetables, tea and red wine with important antioxidant and anti-inflammatory properties, intervening in the modification metabolism and in improving cellular signaling [29, 30]. Geleijnse, J.M. et al., [2002] found that an increased intake of tea, high in flavonoids, prevents primary cardiac ischemia and reduces the risk of death from coronary heart disease, and isoflavones contained in soy cause vasodilation, improve endothelial function and reduce blood pressure [31, 32]. Among the major carotenoids, lycopene is the most powerful antioxidant, contained in large quantities of tomatoes, red fruits, papaya, red pepper and watermelon. Agarwal, S. and Rao, A.V., 2000;

Cruz, R.B. et al., 2013; Jacques, P.F. et al., [2013] found an association between the consumption of lycopene-rich products and the decrease in the incidence of myocardial infarction, coronary heart disease and angina pectoris [33-35]. In addition, Wolak, T. and Paran, E. [2013] found a low plasma level of lycopene in hypertension, acute myocardial infarction, stroke and atherosclerosis [36].

Anti-obesity effect

Obesity is caused by a dysfunction of the gene responsible for the synthesis of proteins in adipocytes. Studies have shown that the administration of anthocyanin-rich preparations to laboratory animals, especially cyanidin, cyanidin-3-glucoside and dolphinidine, results in the expression of these genes resulting in decreased body weight, regulation of hyperglycaemia, hyperinsulinemia and decreased levels of acidity. and the concentration of triacylglycerols in the liver, independent of food intake [37-39].

Neuroprotective effect

Numerous pieces of evidence have suggested that one of the triggers for neurodegenerative disorders, including Alzheimer's disease (AD), is oxidative stress. Kim, S.M. et al., [2012] reported the neuroprotective benefits against hydrogen peroxide-induced cell death of three anthocyanins isolated from black soybean plants, cyanidin-3-glucoside, delphinidin-3-glucoside and petunidin-3-glucoside, by decreased intracellular ROS levels in a dose-dependent manner [40].

Aglicone also has positive results against the oxidative stress induced by hydrogen peroxide. Its administration causes a significant increase in antioxidant activity in the cytosol and cell membranes and an inhibition of DNA fragmentation, induced by hydrogen peroxide [41, 42].

Anti-cancer and anti-angiogenic effect

Angiogenesis is the key to the development of different types of cancer, which is an important step in the transition from a benign to a malignant tumor. In cancer prevention, antiangiogenesis is the process that prevents the formation of new blood vessels, which supply oxygen to tumor cells. Important sources of phytochemicals, including flavonoids and anthocyanins, have been detected and extracted from various plant sources to investigate their anticancer capacity in the colon, esophagus, liver, breast, liver and prostate.

Thus, lycopene, due to its unsaturated nature, is a powerful antioxidant, being used successfully in the treatment of prostate, adrenal and skin cancer, by reducing the level of oxidative stress [43].

Wang, L.S. et al., [2009] found that supplementing the diet given to F344 rats with 5% lyophilized black raspberry inhibits cell proliferation, inflammation, angiogenesis, and induces apoptosis in both preneoplastic and papillomatous esophageal tissue [44]. Another study, [45] suggests that the administration of anthocyanins by supplementing the diet of rats with purple potato extract has a protective effect against colorectal cancer by stopping the cell cycle, cell proliferation and triggering apoptotic mechanisms. Similarly, oral administration of anthocyanin-enriched black rice extract to rats has a protective effect in breast cancer by suppressing angiogenesis and triggering apoptotic mechanisms by depolarizing mitochondrial membranes and releasing cytochrome C into the cytosol [46].

Antimicrobial effect

A number of polyphenolic compounds play an important role in inhibiting the development of pathogens, especially those involved in food [47].

For example, some studies have shown that extracts from maqui beans inhibit the action of the genera *Aeromonas hydrophilia* and *Listeria innocua*, pathogenic bacteria involved in the deterioration of refrigerated foods [48, 49].

Côté, J. et al., [2011] observed that blueberry extract, due to its specific bioactive components such as anthocyanins and flavonols, has high antibacterial activity against *Enterococcus faecium, Pseudomonas aeruginosa, Staphylococcus aureus* and *Escherichia coli* species. and blueberry extract, raspberries, blackcurrants and strawberries, inhibit Gram-negative bacteria, but do not inhibit Gram-positive ones [50]. This variation is due to the difference in the structure of the cell wall between the two species of bacteria, in which the outer membrane of Gram-negative bacteria acts as a selective barrier against hydrophobic compounds, but not on hydrophilic compounds [51, 52].

Prevention and treatment of muscle atrophy

The imbalance of protein homeostasis at the muscular level, as a result of an unhealthy

lifestyle, the installation of the aging process, genetics, the presence of systemic pathologies (inflammation, diabetes, cancer), the use of long-term drug therapies (glucocorticoids), leads at the onset of muscle atrophy, characterized by muscle weakness, loss of muscle mass, disability and last but not least affect the quality of life [53-55]. Numerous evidence from preclinical studies has shown that some nutraceuticals such as proteins, polyphenols, flavonoids, alkaloids, probiotics, used in the long term, have beneficial effects on muscle fibers, maintaining health and intervening in inhibiting the installation of skeletal muscle atrophy [56, 57].

Dietary supplementation with glutamine-rich products prevents rats, skeletal muscle atrophy induced by glucocorticoids and increases muscle mass by inhibiting myostatin expression [58], and inhibits taurine, a non-essential amino acid with a significant sulfur content. muscle atrophy, induced by cisplatin, by restoring mitochondrial function and microtubules [64].

Curcumin, a lipophilic polyphenol and bioactive ingredient of turmeric, improves streptozotocin-induced diabetes, muscle atrophy and promotes muscle health by inhibiting the expression of two MAFbx and MuRF1 genes responsible for atrophy (Ono et al., 2015). At the same time, it has been found that curcumin is involved in increasing the number of muscle fibers and decreases the proteolysis of muscle fibers in rats subjected to hypobaric hypoxia (Chaudhary et al., 2019). Oral administration of resveratrol-rich products, a natural antioxidant found mainly in grapes, has been shown to inhibit muscle protein degradation and attenuate skeletal fiber atrophy in various diseases such as cancer and diabetes [65]. Recently, some studies have reported that astaxanthin, a natural carotenoid with strong antioxidant properties, derived from freshwater algae prevents in rats, induced muscle atrophy by protecting mitochondrial function and attenuating oxidative stress [59].

Flavonoids, a class of benzo-gamma-pyron derivatives (flavonols, isoflavones, calcones, flavones, flavanols, anthocyanins, etc.) abundant in food and plants are characterized by important anti-inflammatory and antioxidant properties [60]. Among them, apigenin found in parsley, celery and grapefruit, relieves obesity-induced muscle atrophy and increases endurance [61]. Dietary supplementation with quercetin, a flavonoid present in citrus fruits, apples, buckwheat, onions, inhibits inflammatory processes and prevents skeletal muscle atrophy by inhibiting the expression of TNF-α and monocyte chemoattractant protein 1 [62]. In addition, quercetin increases the level of the protein hemoxygenase-1 by activating erythroid 2 nuclear translocation factor (Nrf2) and inhibits the action of NF-B in myotubes [63].

Although, in recent decades, the cellular and molecular mechanisms that cause muscle atrophy and the beneficial effects of certain nutraceutical compounds used in the prevention of this condition have been extensively studied, there are still a number of questions regarding the doses used and bioavailability. certain compounds on the metabolism of the whole organism.

5. Conclusions

The growing interest among consumers in quality and prolongation of life has now led to an increase in demand for products with a high content of biologically active compounds at the interface between food and medicine, generically called nutraceuticals. The idea of designing these products, in the form of extracts, tablets or powders and their medical benefits, in preventing and reducing the risk of disease, is due to their action on various cellular structures, by combating oxidative stress and combating the accumulation of free radicals in the body.

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