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THE EFFECT OF BROCCOLI SPROUTS ON DIABETES MELLITUS AND THE GASTROINTESTINAL TRACT

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Abstract. All over the world preference is given to natural plant products, as medicines and vegetables for the prevention and treatment of various diseases due to their less painful effects. Epidemiological studies have shown that natural foods strengthen the immune system and act as anti-inflammatory, antioxidant, anti-mutagenic and anti-cancer agents, one such agent is the miracle vegetable broccoli and broccoli sprouts from the Brassicaceae family. These plants are quite unique due to their content of bioactive metabolites, consisting of a large number of sulfur-containing compounds, such as glucosinolates - sulforaphane, together with phenolic acids and flavonoids.

Keywords: broccoli, broccoli sprouts, sulforaphane, glucosinolates, wide application in medicine.

ВЛИЯНИЕ РОСТКОВ БРОККОЛИ НА САХАРНЫЙ ДИАБЕТ И ЖЕЛУДОЧНО-КИШЕЧНЫЙ ТРАКТ

Аннотация. Во всем мире предпочтение отдается натуральным растительным продуктам, лекарствам и овощам для профилактики и лечения различных заболеваний в связи с их менее болезненным действием. Эпидемиологические исследования показали, что натуральные продукты укрепляют иммунную систему и действуют как противовоспалительные, антиоксидантные, антимуtagenные и противораковые средства, одним из таких средств является чудо-овощ брокколи и ростки брокколи из семейства Brassicaceae. Эти растения достаточно уникальны благодаря содержанию в них биоактивных метаболитов, состоящих из большого количества серосодержащих соединений, таких как глюкозинолаты - сульфорафан, вместе с фенолокислотами и флавоноидами.

Ключевые слова: брокколи, ростки брокколи, сульфорафан, глюкозинолаты, широкое применение в медицине.

INTRODUCTION

All over the world preference is given to natural plant products, as medicines and vegetables, since the ancient medical system, such as Ayurveda, has been used for many years to treat various diseases. In recent years, much attention has been paid to herbal products for the prevention of various diseases due to their less painful effects.

MATERIALS AND METHODS

Epidemiological studies have shown that natural foods strengthen the immune system and act as anti-inflammatory, antioxidant, anti-mutagenic and anti-cancer agents, one of these agents is the miracle vegetable broccoli and broccoli sprouts [1].

Broccoli (*Brassica oleracea* var. *Italica* plenck) is an annual vegetable plant belonging to the cabbage family. Like many other medicinal plants, broccoli is a good source of various phytochemicals. This variety of cabbage is considered a natural anti-cancer anti-carcinogenic vegetable and it is known in folk and traditional medicine due to the presence of high concentrations of indole-3-carbinol (I3C) and sulforafan, which is used to treat breast cancer and a number of other diseases[2;3;4;5].



Figure 1: Broccoli sprouts

Microgreens, edible sprouts of vegetables and herbs, have received increasing attention in recent years and are considered functional foods or superfoods for their valuable health-promoting properties. In particular, 3-day-old broccoli sprouts (*Brassica oleracea* L. var. *Italica*) are highly valued for their significant content of 10-100 times more glucoraphanin (sulforaphane glucosinolate) than the corresponding mature plants. Notably, the sprouts of many broccoli cultivars contain negligible amounts of indole glucosinolates, which predominate in mature vegetables and can produce degradation products (eg, indole-3-carbinol) that can enhance tumorigenesis. Therefore, a small amount of cruciferous sprouts can protect against cancer risk just as effectively as a much larger amount of mature vegetables of the same variety. [6;7]

Nutrition plays an important role in health and disease; Some nutrients are not only essential, but important for optimal health. Traditionally, food is considered as a source of energy, which, thanks to its nutrients, can maintain homeostasis. However, it is now recognized that certain types of foods, known as functional foods, can provide more than just energy and essential nutrients [8].

RESULTS

Sulforaphane was described in the middle of the last century as an antibiotic and was isolated from red cabbage and from the grazing watercress weed in the western United States. It has since been synthesized by various groups, but Talalay and Zhang were the first to isolate it from broccoli and demonstrate its anti-cancer properties. Its biogenic precursor, glucoraphanin, was then found to be abundant in broccoli sprouts, and sulforaphane activity was confirmed in animal models of carcinogenesis. An evaluation of the structure and activity of a series of more

than 100 synthetic analogs made by Posner and colleagues did not reveal a more powerful inducer of cytoprotective enzymes (Phase 2) than sulforaphane [9].

In raw broccoli sprouts, sulforaphane (SFN) exists in the biologically inactive form of sulforaphane glucosinolates (SGS). The transformation of SGS into SFN occurs during chewing, where SGS is exposed to the action of myrosinase, which is also a component of broccoli sprouts [10].

Sulforaphane (SFN), an organosulfur compound, belongs to the group of isothiocyanates (ITC) and is mainly found in cruciferous vegetables. Several studies have shown that SFN has a broad spectrum of activity and has shown exceptional potential as an antioxidant, anticancer, antiangiogenic, and anti-inflammatory agent. In addition, SFN has been proven to be less toxic, non-oxidizing, and its administration to humans is well tolerated, making it an effective natural dietary supplement for clinical trials. SFN has shown its ability to be a promising future drug molecule for the treatment of various diseases, mainly due to its powerful antioxidant properties [11].

Extensive work by Talalay and colleagues has characterized the pharmacokinetics and safety in humans of oral ingestion of sulforaphane-rich (SFR) or glucoraphanin-rich (GRR) hot water extracts prepared from broccoli sprouts [12].

Broccoli-derived sulforaphane is emerging as a phytochemical with this ability, oral doses of which are able to favorably modify genes associated with chemoprevention. Compared to widely used phytochemical-based supplements such as curcumin, silymarin, and resveratrol, sulforaphane more potently activates Nrf2, inducing the expression of a set of cytoprotective genes [13].

In many cases, freeze-dried standardized extracts of seedlings from specially selected varieties and seed sources grown in a routine manner have been used to ensure drug consistency in many studies. First of all, these studies established the safety of these drugs glucoraphanin and sulforaphane. Dose limiting factors are taste, gastric irritation and flatulence. Second, they demonstrated linear uptake and elimination of sulforaphane after a wide range of doses in the form of a sulforaphane drink. Third, the bioavailability of sulforaphane was significantly better when taken as a sulforaphane drink compared to a glucoraphanin drink. This last result indicates the limited ability of human intestinal microbial thioglucosidases to catalyze the conversion of glucoraphanin to sulforaphane [14].

Isothiocyanates from cruciferous vegetables have been extensively studied in cells and animals for their preventive and therapeutic effects. However, the transfer of their usefulness to the human population has been limited and difficult. This paper summarizes and discusses clinical trials using two isothiocyanates, sulforaphane (SFN; 1-isothiocyanato-4-(methylsulfinyl)butane) and phenethylisothiocyanate (PEITC; 2-isothiocyanatoethylbenzene), which are isolated primarily from broccoli and watercress, respectively. Both of these compounds have been used in small human clinical trials, either in food matrices or as single agents against diseases ranging from cancer to autism. [15].

Type II diabetes, mainly caused by insulin resistance or minor damage to the pancreas, is characterized by hyperglycemia. With the development of insulin resistance, the level of glucose in the blood does not increase significantly until the β -cells of the islets are damaged and insulin secretion begins to decrease [16].

Type 2 diabetes is becoming more common worldwide and not all patients can be successfully treated with existing drugs. Axelsson et al. analyzed the expression patterns of genes associated with type 2 diabetes and compared them to the gene signatures of thousands of drug candidates to find compounds that could counteract the effects of diabetes. The lead candidate in this analysis was sulforaphane, a natural compound found in broccoli and other vegetables. The authors showed that sulforaphane inhibits glucose production in cultured cells and improves glucose tolerance in rodents on diets high in fat or fructose. In addition, in clinical trials, broccoli sprout extract containing sulforaphane was well tolerated and improved fasting glucose levels in obese patients with uncontrolled type 2 diabetes [17].

High glucose production of reactive oxygen intermediates and inflammatory damage are recognized causes of nerve dysfunction and subsequent damage in diabetic neuropathy. Sulforaphane, a well-known chemotherapeutic agent, shows promise in diabetic neuropathy due to its dual antioxidant and anti-inflammatory activities. The present study investigated the effect of sulforaphane on streptozotocin (STZ)-induced diabetic neuropathy in rats. For in vitro experiments, neuro2a cells were incubated with sulforaphane in the presence of normal (5.5 mM) and high glucose (30 mM). In in vivo studies, sulforaphane (0.5 and 1 mg/kg) was administered six weeks after diabetes induction for two weeks. Motor nerve conduction velocity (MNCV), sulforaphane improved nerve blood flow (NBF) and pain, and malondialdehyde (MDA) levels were reduced [18].

The results showed that SFN has an anti-diabetic effect by attenuating non-alcoholic fatty liver disease and repairing pancreatic tissue, in combination with modulation of the intestinal microbiota. Alleviation of non-alcoholic fatty liver disease with SFN was accompanied by an increase in the antioxidant capacity of the liver and improved resistance to FGF21 [19].

We have found that sulforaphane [(-)-1-isothiocyanato-(4R)-(methylsulfinyl)butane], isothiocyanate, abundant as a glucosinolate precursor in some broccoli cultivars and broccoli sprouts, is a potent bacteriostatic agent against 3 reference strains and 45 clinical isolates of *H. pylori* [minimum inhibitory concentration (MIC) for 90% of strains ≤ 4 $\mu\text{g/ml}$], regardless of their resistance to conventional antibiotics. In addition, short-term exposure to sulforaphane was bactericidal and eliminated intracellular *H. pylori* from a human epithelial cell line (HEp-2). In additional experiments, sulforaphane blocked benzo[a]pyrene-induced pancreatic tumors in ICR mice. This protection resulted from the induction of phase 2 detoxification and antioxidant enzymes and was abolished in mice lacking the *nrf2* gene, which regulates phase 2 enzymes. Thus, the dual action of sulforaphane in inhibiting *H. pylori* infection and blocking gastric tumor formation offers hope that these mechanisms may act synergistically to provide diet-based protection against gastric cancer in humans [20].

DISCUSSION

These studies of *H. pylori* infection clearly demonstrated that SFN inhibits *H. pylori* viability both in vitro and in vivo and also alleviates *H. pylori*-induced gastritis in mice and humans. Similarly, our study of NSAID-induced small bowel injury showed that SFN not only mitigated aspirin-induced injury to small bowel epithelial cells in vitro, but also improved indomethacin-induced small bowel injury in mice in vivo [21].

The tartronic acid contained in broccoli inhibits the conversion of carbohydrates into fats and cholesterol in overweight and obesity. The use of such drugs and dietary supplements is recommended in the treatment of gastric ulcer and duodenal ulcer, cleansing the body of toxins,

eliminating dysbacteriosis, flatulence and dyspepsia. Juice from fresh leaves is also recommended for these diseases. With peptic ulcer of the stomach and duodenum, pain disappears or decreases, vomiting, nausea, heartburn, and constipation stop. In diseases of the liver (hepatitis, angiocholitis), dyspepsia disappears (digestion disorders), appetite improves. *Helicobacter pylori* infection is the most important etiological factor in almost all non-drug gastric and duodenal ulcers. Scientific research and experience in the use of broccoli in these pathologies shows high efficiency, including antibiotic-resistant forms of *Helicobacter pylori* [22].

CONCLUSIONS

Brassicaceae vegetables are quite unique due to the content of bioactive metabolites, consisting of a large number of sulfur-containing compounds such as glucosinolates, along with phenolic acids and flavonoids.

.Multiple in vitro and in vivo studies have shown that broccoli sprouts have various biological properties, including antioxidant, antitumor, anticancer, antimicrobial, anti-inflammatory, anti-obesity and anti-diabetic properties

Preventive trials of whole foods or simple extracts hold promise for effectively reducing the growing global burden of cancer and, in contrast to promising isolated phytochemicals or pharmaceuticals, cost-effective means. It can be applied to personalized medicine in exactly the same way as to a pharmaceutical approach, but only green chemoprophylaxis can be applied in both rich and poor settings.

Sulforaphane, in turn, is an inducer of cytoprotective enzymes through the activation of Nrf2 signaling and a potent inhibitor of carcinogenesis in several mouse models. Sulforaphane is also protective in models of diabetes, neurodegenerative diseases, and other inflammatory processes, likely reflecting additional Nrf2 actions and interactions with other signaling pathways.

The results suggest the possibility of including them, or more likely, preparations derived from source plants, in larger efforts to mitigate the effects of human diseases. The context of the application of these compounds and plants in evidence-based food and nutrition policy is also assessed.

As such, Brassicaceae plants represent an excellent source of health-promoting nutrients and phytochemicals, which generally contributes to the dietary importance of these food crops as beneficial against certain types of disease. Then their consumption should be actively promoted.

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