



Phytonutrients: Recent advances in health benefits

Kachhot S K¹, Patel B G²

¹ Department of Food Science and Nutrition, CAN & CS, Sardarkrushinagar Dantiwada Agricultural University, Sardarkrushinagar, Gujarat, India

² Professor and Head, Department of Food Science and Nutrition, ACN&CS, Sardarkrushinagar Dantiwada Agricultural University, Sardarkrushinagar, Gujarat, India

Abstract

Plant-based foods contain a variety of nutrients (carbohydrates, proteins, lipids etc.) that can meet almost all our nutritional needs. In addition, there are rich biologically active ingredients in plant-based foods known as "phytonutrients" which have many benefits to human health; these include polyphenols, flavonoids, carotenoids, limonoids, Phytosterols and anthocyanins among others. These active ingredients have special activities affecting human health, such as anti-allergy, anti-diabetes, anti-aging, hypolipidemic and anti-inflammatory. Phytonutrients play a major role in the body by maintaining and modulating immune function to prevent specific diseases. These functional also called as medicinal foods contain phytonutrients or phytomedicines that play beneficial roles in maintaining well-being, enhancing health, and modulating immune function to prevent specific diseases. "Phytonutrients" and "Phytotherapy" is a more recent term that refers to a science of treatment using a group of natural substances that include certain herbs and their derivatives for use as dietary supplements and regulated as foods. This review paper will be summarized about phytonutrients and their recent advances in health benefits.

Keywords: Karpooravalli, overripening, nutribars, tray dries, control panel

Introduction

Phytonutrients or phytochemicals are natural compounds found in all plant foods. They represent a complex group of bioactive and non-nutritive compounds in the plant kingdom and are an essential part of the human diet.

Phytonutrients act as attractants for pollination or as protective agents against attacks by insects and parasites or exposure to various stresses such as ultraviolet light (Zaynab *et al.*, 2018) [36]. In addition, phytonutrients influence the color, taste and aroma of plants and are considered potentially valuable for nutrition and human health. In fact, they are often found in our diet through the consumption of fruits, vegetables, whole grains, nuts, beans, aromatic herbs, tea and coffee (Maggini *et al.*, 2018) [20].

Phytonutrients are considered anti-inflammatory, detoxifying, antioxidant, and hormone-balancing compounds that should be taken daily to prevent disease and maintain optimal health. A balanced diet containing fruits and vegetables of various shapes and colors provides the body with a range of beneficial compounds. "Phytochemicals have antioxidant effects that protect cells from cancer and cardiovascular disease, as well as urinary tract infections, rheumatoid arthritis, and immune system suppression" (Liu, 2003).

Food plays an important role in maintaining the proper functioning of the human body. Due to recent advances in medicine and nutritional sciences, natural products as health-promoting foods are receiving great attention from medical professionals and consumers. Bioactive foods and nutraceuticals have been shown to be potential supplements for the treatment of various diseases and natural food sources for prevention.

Consumers can use nutraceuticals to supplement poor diets, improve overall health, delay the onset of age-related diseases, after illness, for stress, during pregnancy and

weight loss, to improve athletic performance, and to treat symptoms (colds, cough, arthritis, etc.). These functional foods, also called medicinal foods, contain phytonutrients or phytomedicines that play a positive role in maintaining well-being, improving health and modulating immune function to prevent certain diseases. "Phytonutrients" and "Phytotherapy" are newer terms that refer to the science of healing with a group of natural substances, including some herbs and their derivatives that serve as dietary supplements and are regulated as foods.

The human body requires nutrients other than nutrients such as proteins, vitamins and minerals. Phytonutrients have the unique ability to fight free radicals that circulate in the body in search of electrons. By providing electrons, phytonutrients prevent free radicals from stealing electrons from proteins or other nutrients, which is the "theft" that leads to oxidative stress.

Types of phytonutrients

Broad categories have emerged that typically get grouped into three main areas:

- 1. Thiols:** Chemically, a type of mercaptan with a sulfhydryl functional group, often found in Allium. Can protect cells from oxidative damage. Sulfur-containing compounds such as glucosinolates, which include isothiocyanates as a subset.
- 2. Phenols:** Also called phenolics, have a hydroxyl group bonded directly to an aromatic hydrocarbon group. Phenols protect against oxidative damage and inflammation. Includes the broad category of flavonoids with tannins and isoflavones as subsets.
- 3. Terpenes-** Hydrocarbons consisting of isoprene units found in a wide variety of plants. Their functionality depends on their structure, but may provide anti-cancer

and cardiovascular-health properties. Includes the broad category of carotenoids with alpha-carotene, beta-carotene, lutein and lycopene as subsets.

Phytonutrients and Health

- Plants use colors as a protective mechanism, which are also a source of phytonutrients. Along with herbs and spices, phytonutrients form the basis for more than 40% of medicines. They have a healing effect on our body and their defense mechanisms can be used to optimize body functions (Hyman, 2013) ^[10].

Flavonoids

- Flavonoids belong to the polyphenol family and include flavonols, flavones, flavanols, flavanones and isoflavonoids. Flavonoids are found in many plants and are the universal pigments of yellow, red and purple. They are the molecules that give plants their “colorful hues”.
- Flavonoids are found in grapes, blueberries, broccoli, cabbage and many other fruits and vegetables. Flavonoids can prevent heart disease and cancer, lower blood pressure, and destroy some bacteria in foods (Reader's Digest, 2013) ^[25].
- Flavonoids are present in a variety of plants, although in relatively low concentrations. The main sources of flavonoids are tea, onions and apples, but they are also found in many other colorful plants. Flavanones are found in tomatoes, citrus fruits and herbs. Flavonols are found in olives, onions, cabbage and lettuce. Flavones are found in celery and olives. Pears, red wine and tea are good sources of flavonols. Finally, isoflavones are mainly found in soy products (King and Young, 1999) ^[15].
- Flavonoids in berries, black tea, celery, citrus fruits, green tea, olives, onions, purple grapes, purple grape juice, seeds and fruit products from soy, vegetables, whole wheat and wine act as antioxidants, eliminate carcinogens and bind nitrates in the stomach, prevents its conversion into nitrosamines, inhibits cell proliferation, inhibits platelet aggregation and arteriosclerosis.
- In 2015 ^[22], Mastroiacovo *et al.* examined the effects of daily flavanol consumption on cognitive function in a randomized controlled trial of 90 elderly patients. The results of their study showed that daily consumption of a flavonoid-rich drink (993 mg/day) for 8 weeks significantly improved results on exercises to assess cognitive functions, particularly the course test and the verbal fluency.
- The effects of flavonoids were recently demonstrated in a study by Law *et al.* confirmed. After two months of daily treatment with 100 ml of onion juice rich in flavonoids and phenolic acids, osteoporosis patients showed significant improvement in oxidation markers and positive modulation of bone loss. The mechanisms of action were related to the antioxidant properties of flavonoids as well as their ability to slow the differentiation of progenitor cells into osteoclasts (Law *et al.*, 2016) ^[18].

Isoflavones

- Isoflavones, i.e. Flavonoids found in soy may mimic the effects of estrogen and play a role in relieving

menopause symptoms as well as protecting against some hormone-dependent cancers.

- Hachul *et al.*, (2011) ^[8] examined the effect of flavonoids and particularly isoflavones on sleep quality in postmenopausal women suffering from insomnia. Subjects received 80 mg of isoflavones or placebo daily for 4 months. Sleep analysis was performed using polysomnography and questionnaires. The results obtained show a significant decrease in the number of episodes of insomnia at the end of treatment in patients treated with isoflavones versus placebo as well as an improvement in sleep efficiency.
- A systematic literature review of 26 randomized clinical studies and 2652 patients established a therapeutic benefit of isoflavones in the management of bone loss during menopause, with treatment significantly increasing bone density in the lumbar spine and femoral neck (Lambert *et al.*, 2017) ^[17].

Carotenoids

- Carotenoids are another group that include more readily discussed phytochemicals like beta-carotene, lycopene, lutein, and zeaxanthin. They can be found in carrots, tomatoes, and watermelon, and may also reduce the risk of certain cancers, and have strong antioxidant effects.
- Beta-carotene may help prevent night blindness and age-related macular degeneration. It could also potentially protect against some cancers and keep your skin, hair, nails, gums, glands, bones and teeth healthy.
- The best sources of beta-carotene include orange, yellow, and dark green fruits and vegetables such as carrots, sweet potatoes, pumpkin, broccoli, kale, spinach, apricots, peaches, and melons. Lutein and zeaxanthin may protect against cataracts and age-related macular degeneration (Reader's Digest, 2013) ^[25].
- Carotenoids have also shown positive effects on stress management. Kell *et al.* (2017) ^[13] examined the therapeutic benefits of saffron, including its crocin (carotenoid) content, in the treatment of mood, stress and anxiety disorders. After 4 weeks of treatment with saffron at a dose of 28 mg/day, patients noted lower levels of stress and anxiety, as well as significant improvement in mood, compared to placebo. Another study by Stringham *et al.* (2018) ^[27] attempted to demonstrate the benefit of long-term carotenoid supplementation for stress management.
- Carotenoids, especially their anti-inflammatory effects, have therapeutic importance in the prevention of chronic joint diseases. A prospective study by Pattison *et al.* In 2005 ^[24], more than 25,000 people studied the effects of carotenoid consumption on the risk of developing rheumatoid arthritis and concluded that increasing the consumption of β -cryptoxanthin in an amount equivalent to one glass of orange juice reduced the risk of the development of this pathology reduces the antioxidant activity properties of this phytonutrient.
- Carotenoids are also of interest in the health field, particularly in problems related to fatigue and recovery. A randomized, controlled clinical trial conducted by Imai *et al.* in 2018 ^[11] examined the benefits of the antioxidant properties of carotenoids in treating fatigue. Their work was to evaluate the effect of supplementation with 3 mg of astaxanthin and 5 mg of

sesamin for 4 weeks on mental fatigue. At the end of treatment, they observed a significant reduction in mental fatigue compared to placebo and a smaller increase in circulating levels of phosphatidylcholine hydroperoxide, a marker of oxidative stress.

Lycopene

- Lycopene may also protect against some types of cancer (prostate, stomach and lung). Food sources include tomatoes, pink grapefruit, watermelon, and pink guava.
- Ghavipur *et al.*, (2013) studied a group of 106 overweight or obese female students at Tehran Medical University who were randomly assigned to drink 330 ml of tomato juice or water per day for twenty days. Compared to the control group and baseline, IL-8 and TNF- α serum concentrations were significantly reduced in overweight and obese women.
- In another study on tomato juice conducted by Tsitsimpikou *et al.*, (2014) [29]. The researcher found that people with metabolic syndrome noticed significant improvements in inflammation and endothelial dysfunction after drinking tomato juice four times a week for two months, compared to a control group.

Caffeine

- Caffeine is a molecule from the alkaloid family. In contrast, caffeine is considered a family of its own because it forms an important part of your daily phytonutrient intake and its health benefits are well documented.
- Caffeine is the most commonly consumed psychoactive substance in the world. It is found in coffee, kola nuts, tea or mate leaves.
- White *et al.*, (1980) [33] examined the effects of caffeine on muscle tension and anxiety. Their work showed that heavy coffee drinkers who were deprived of caffeine for three hours saw their muscle tension and anxiety significantly increase compared to light coffee drinkers, and that caffeine consumption had these effects. Effects. The parameters return to the values observed in placebo-treated patients.
- The literature review by Grosso *et al.*, (2016) [7], which included 12 clinical observational studies, also examined the effects of coffee, tea, and caffeine consumption on depression. The results of this analysis suggest that daily consumption of caffeinated coffee may play a protective role in depressive symptoms in a nonlinear dose-response relationship, and the maximum effect is achieved with daily consumption of 400 ml of coffee. According to the authors, this effect could be due to caffeine's stimulation of the central nervous system and improvement of dopaminergic neurotransmission.
- A Cochrane review by Welsh *et al.*, (2010) [32] examined the effect of caffeine on respiratory parameters in asthma patients. An analysis of seven randomized clinical trials involving 75 subjects showed significant improvement in respiratory parameters for up to 4 hours, even at doses below 5 mg/kg.

Anthocyanins

- Anthocyanins are a subfamily of flavonoids and are formed as a result of general flavonoid metabolism. The

most popular anthocyanins are found in red, pink, blue or purple fruits and vegetables.

- Anthocyanins are concentrated primarily in cherries, berries (such as black currants, elderberries and blueberries) and plums. They are also found in root vegetables such as beets and radishes, red onion bulbs, and in drinks such as fruit juices and red wine (Lin *et al.*, 2017) [20].
- Biedermann *et al.*, (2013) [3] showed that anthocyanins appear to be active in the treatment of ulcerative colitis by reducing some symptoms and the endoscopic Mayo score. This effect may be related to the anti-inflammatory activity of anthocyanins, which leads to a reduction in tumor necrosis factor α (TNF- α) and IFN γ levels in mesenteric lymph nodes.
- The influence of anthocyanins on the cognitive parameters of the elderly population was reported by Calapai *et al.* (2017) [4]. This randomized, double-blind, placebo-controlled study evaluated the effect of anthocyanin supplementation at a dose of 250 mg/day for 12 weeks using a battery of cognitive tests. The results showed significant improvements in attention, language and memory with anthocyanins compared to placebo, as well as lower frequencies of anxiety and depression, which could be explained by their antioxidant, anti-inflammatory and anti-apoptotic properties.

Organicsulfur compounds

- Organicsulfur compounds include several classes of molecules with similar basic chemical structures. The family of organosulfur compounds includes isothiocyanates, indoles, compounds derived from allyl sulfides, and sulforaphanes. The two most common organosulfur compounds in plant foods are glucosinolates and sulfur derivatives of garlic. Sulforaphane is found primarily in cruciferous vegetables (cabbage and broccoli), and isothiocyanate is found in mustard seeds. Garlic is also a good source of sulfur compounds.
- Organicsulfur compounds also have therapeutic importance for antiviral protection. In 2016 [23], Muller *et al.* examined the effect of administration of sulforaphane-rich broccoli on the immune system's response to influenza vaccination. Their results indicate a significant decrease in the number of natural killer T cells (NKT), T and N cells, as well as a significant increase in granzyme B (antiviral protein) production compared to the placebo group, suggesting that sulforaphanes bring about an improvement. to ward off viral infections.
- The antioxidant activity of organosulfur compounds, particularly glucophanes, has been shown to improve liver function in fatty liver patients after 4 months of treatment, probably due to their antioxidant properties and their ability to stimulate detoxification enzymes through activation of the transcription factor NRF2 (Kikuchi *et al.*, 2015) [14].
- In the study by Yanaka *et al.*, (2018) [34], the use of glucosinolates, especially sulforaphanes, contained in broccoli sprouts, when consumed daily at a dose of 20 g/day, allowed a significant reduction in constipation compared to placebo. for example 4.4 mg/day sulforaphane) for 21 days. According to the authors,

this effect results from the antioxidant effect of sulforaphanes on the gastrointestinal tract.

- Kaczmarek *et al.*, (2019) ^[12] attributed the positive effects of organosulfur compounds in the gastrointestinal tract to a direct effect on the intestinal flora.

Tannins

- Tannins, like flavonoids, belong to the family of phenolic compounds. Plums, cocoa beans, tea and wine as well as pomegranate peels, sorghum and barley seeds contain large amounts of tannins.
- Tannins, found in black-eyed peas, grapes, lentils, red and white wine, and tea, may inhibit the activation of carcinogens, promote cancer, and act as antioxidants.
- Tannins have also shown therapeutic value in the treatment of digestive disorders. In 2018, Venancio *et al.*, examined the benefits of consuming 300g of mango, rich in gallotannins, daily in volunteers suffering from chronic constipation. After 4 weeks of treatment, an improvement in functional parameters (frequency and consistency of bowel movements) and inflammatory parameters was demonstrated.
- Tannins, particularly crofelemer, were also investigated for the treatment of symptoms associated with irritable bowel syndrome in a large randomized controlled trial by Mangel and Chaturvedi (2008) ^[21]. After 3 months of treatment, functional parameters did not improve, but abdominal pain and discomfort improved significantly in women treated with 500 mg of the product.
- Tannins have therapeutic importance in the areas of energy and vitality, as they have been proven to reduce fatigue and improve physical performance. In a randomized controlled trial by Ataka *et al.* in 2007 ^[1], daily consumption of a tannin-rich extract (1,200 mg) for 8 days resulted in improved resistance to exercise-induced fatigue compared to placebo, without altering cardiovascular parameters.

Phenolic acids

- Phenolic acids or phenolcarboxylic acids belong to the polyphenol family and are among the most common nonflavonoid plant phenolic compounds. Phenolic acids are found in many foods, such as cereals, wheat flour, onions, coffee, kiwi, berries, apples and citrus fruits. In addition to dietary sources, phenolic acids can also arise from the secondary metabolism of other types of polyphenols by the colonic microflora.
- The effect of flavonoids was demonstrated in a study by Law *et al.*, (2016) ^[18]. After two months of daily treatment with 100 ml of onion juice rich in flavonoids and phenolic acids, osteoporosis patients showed significant improvement in oxidation markers and positive modulation of bone loss. The mechanisms of action were related to the antioxidant properties of flavonoids and their ability to slow the differentiation of progenitor cells into osteoclasts.
- Randomized controlled clinical trial conducted by Wattanathorn *et al.*, (2018) ^[31] reported that daily consumption of 1.5 g of a phenolic acid-rich extract for 8 weeks significantly increased the number of markers involved in bone formation (osteocalcin, alkaline phosphatase) and reduced resorption cross-links (β -terminated carboxyl of collagen) in comparison to the basic value.

Curcuminoids

- The most important curcuminoids are curcumin. Curcumin is considered the most important bioactive phytochemical in turmeric and makes up about 5% of the rhizome. Some other bioactive compounds present in turmeric essential oils.
- Turmeric is widely cultivated in Southeast Asia and the Indian region, where it is used primarily for medicinal purposes, as a dietary supplement, and for culinary purposes. The most important component of turmeric, used as a spice and herbal supplement, is the rhizome, which is found in the roots of the plant. Turmeric powder has a pungent taste and a characteristic yellow-orange color due to the curcuminoid pigments and phytochemicals contained in the rhizome (Hossain and Ishimine, 2005) ^[9].
- Li *et al.*, (2018) reported that curcumin extracts (200 mg/kg) produced tumor growth inhibition and anti-metastatic effects *in vivo* using CT26, HT29 and HCT116 colon cancer cells. In addition, in combination with the phytochemical quercetin, it has a synergistic effect against lung, skin, colon and breast cancer cells.
- In a very recent systematic review, Kunnumakkara *et al.*, (2021) ^[16] explained the potential of curcumin and other spices in combating SARS-COV-2 due to their anti-inflammatory and cytokine storm-inhibiting properties. These results suggest that turmeric extracts may represent not only a potential treatment but also an alternative for preventing viral infections.
- Another important effect of turmeric is its antifungal effect. Chen *et al.*, (2018) ^[5] showed that turmeric extracts have a strong antifungal effect against 20 pathogenic fungi (e.g. *Fusarium verticillioides*, *Curvularia pallescens*, *Colletotrichum falcatum*, *Aspergillus niger*, *Aspergillus terreus*, *Fusarium oxysporum*, *Fusarium moniliforme*, *Fusarium graminearum*, *Phoma wasabiae*, *Alternaria alterna*, *Botrytis cinere*, *Chaetomium oloviceum*, *Peniconium*, *Botrytis cinere*, *Chaetomium olivivios* and *Verticillium dahlia*) interruption of the synthesis of the main components of the fungal cell wall and disruption of protein synthesis. This study concluded that turmeric phytochemicals in combination have better antifungal effects than individual compounds.

Allicin

- Allicin is the most important bioactive phytochemical in aqueous garlic extract and is also responsible for the characteristic smell of garlic. Therefore, the enzyme alliinase converts allicin to alliin when garlic cloves are cut/crushed. For this reason, several studies have shown that minced fresh garlic can provide the most active phytochemicals.
- Garlic is composed of various phytonutrients, including alkaloids, saponins, flavonoids, tannins, phenols, terpenoids, and organic sulfides. In addition, garlic is considered a good source of vitamins and minerals, including vitamins B1, B6, C, manganese, copper, phosphorus, selenium and calcium (Saif *et al.*, 2020) ^[26].
- Interestingly, phytochemicals such as garlic allicin have been combined with commonly used cancer drugs to enhance the therapeutic effects of current treatments. A study by Țigu *et al.* conducted experiment in (2020) ^[28]

showed that the combination of the anticancer drug 5-fluorouracil with allicin inhibits the migration and proliferation of colorectal (DLD-1) and lung cancer cells (SK-MES-1) as well as proliferation *in vitro*.

- The phytochemicals contained in garlic also have an antioxidant effect. Bhatt and Patel (2013) [2] prepared 900 mg of cooked or raw garlic and incubated these samples with gastric enzymes. These results showed that cooked garlic lost 90% of its phenolic content, resulting in lower antioxidant activity due to heat (evaporation of the active ingredient) compared to raw garlic.
- In a double-blind clinical study by Zare *et al.*, (2019) [35] examined the anti-inflammatory effect in 40 peritoneal dialysis patients by administering garlic extract twice daily for 8 weeks. The results showed that garlic reduced inflammatory markers in patients with end-stage renal disease, particularly interleukin-6, C-reactive protein and erythrocyte sedimentation rate in the treatment group.

Conclusion

- Regular consumption of foods rich in phytochemicals, such as fruits and vegetables, whole grains, etc., is strongly associated with a reduced risk of developing chronic diseases such as cancer and cardiovascular disease. Therefore, a diet rich in colorful fruits and vegetables is highly recommended for health, well-being and possible disease prevention.

References

1. Ataka S, Tanaka M, Nozaki S, Mizuma H, Mizuno K, Tahara T, *et al.* Effects of Applephenon and ascorbic acid on physical fatigue. *Nutrition*,2007;23:419–423.
2. Bhatt A, Patel V, Antioxidant activity of garlic using conventional extraction and *in vitro* gastrointestinal digestion. *Free Radic Antioxid*,2013;3(1):30-34.
3. Biedermann L, Mwinyi J, Scharl M, Frei P, Zeitz J, *et al.* Bilberry ingestion improves disease activity in mild to moderate ulcerative colitis—An open pilot study. *J Crohns Colitis*,2013;7:271–279.
4. Calapai G, Bonina F, Bonina A, Rizza L, Mannucci C, *et al.* A randomized, double-blinded, clinical trial on effects of a *Vitis vinifera* extract on cognitive function in healthy older adults. *Front Pharmacol*,2017;8:776.
5. Chen C, Long L, Zhang F, Chen Q, Chen C, *et al.* Antifungal activity, main active components and mechanism of *Curcuma longa* extract against *Fusarium graminearum*. *PLoS One*,2018;13(3):e0194284.
6. Ghavipour M, Saedisomeolia A, Djalali M, *et al.* Tomato juice consumption reduces systemic inflammation in overweight and obese females. *Br J Nutr*,2013;109(11):2031–2035 *et al.*
7. Grosso G, Micek A, Castellano S, Pajak A, Galvano F, *et al.* Coffee, tea, caffeine and risk of depression: A systematic review and dose-response meta-analysis of observational studies. *Mol Nutr Food Res*,2016;60:223–234.
8. Hachul H, Brandão LC, D’Almeida V, Bittencourt LR, Baracat EC, *et al.* Isoflavones decrease insomnia in postmenopause. *Menopause*,2011;18:178–184.
9. Hossain MA, Ishimine Y, Growth, yield and quality of turmeric (*Curcuma longa* L.) cultivated on dark-red soil, gray soil and red soil in Okinawa, Japan. *Plant Prod Sci*,2005;8(4):482-486.
10. Hyman M, Eat your medicine: Food as pharmacology.2013.
11. Imai A, Oda Y, Ito N, Seki S, Nakagawa K, *et al.* Effects of dietary supplementation of Astaxanthin and Sesamin on daily fatigue: A randomized, double-blind, placebo-controlled, two-way crossover study. *Nutrients*,2018;10:281.
12. Kaczmarek JL, Liu X, Charron CS, Novotny JA, Jeffery EH, *et al.* Broccoli consumption affects the human gastrointestinal microbiota. *J Nutr Biochem*,2019;63:27–34.
13. Kell G, Rao A, Beccaria G, Clayton P, Inarejos-García AM, *et al.* Affron® a novel saffron extract (*Crocus sativus* L.) improves mood in healthy adults over 4 weeks in a double-blind, parallel, randomized, placebo-controlled clinical trial. *Complement Ther Med*,2017;33:58–64.
14. Kikuchi M, Ushida Y, Shiozawa H, Umeda R, Tsuruya K, *et al.* Sulforaphane-rich broccoli sprout extract improves hepatic abnormalities in male subjects. *World J Gastroenterol*,2015;21:12457–12467.
15. King A, Young G, Characteristics and occurrence of phenolic phytochemicals. *J Am Diet Assoc*,1999;99:213–218.
16. Kunnumakkara AB, Rana V, Parama D, Banik K, Girisa S, *et al.* Covid-19, cytokines, inflammation, and spices: How are they related? *Life Sci*,2021;119-201.
17. Lambert MNT, Hu LM, Jeppesen PB, A systematic review and meta-analysis of the effects of isoflavone formulations against estrogen-deficient bone resorption in peri- and postmenopausal women. *Am J Clin Nutr*,2017;106:801–811.
18. Law YY, Chiu HF, Lee HH, Shen YC, Venkatakrishnan K, *et al.* Consumption of onion juice modulates oxidative stress and attenuates the risk of bone disorders in middle-aged and post-menopausal healthy subjects. *Food Funct*,2016;7:902–912.
19. Lin BW, Gong CC, Song HF, Cui YY. Effects of anthocyanins on the prevention and treatment of cancer. *Br J Pharmacol*,2017;174:1226–1243.
20. Maggini S, Pierre A, Calder PC, Immune function and micronutrient requirements change over the life course. *Nutrients*,2018;10:1531.
21. Mangel AW, Chaturvedi P, *et al.* Evaluation of crofelemer in the treatment of diarrhea-predominant irritable bowel syndrome patients. *Digestion*,2008;78:180–186.
22. Mastroiacovo D, Kwik-Urbe C, Grassi D, Necozone S, Raffaele A, Pistacchio L, *et al.* Cocoa flavanol consumption improves cognitive function, blood pressure control, and metabolic profile in elderly subjects: The Cocoa, Cognition, and Aging (CoCoA) Study—A randomized controlled trial. *Am J Clin Nutr*,2015;101:538–548.
23. Muller L, Meyer M, Bauer RN, Zhou H, Zhang H, Jones S, *et al.* Effect of broccoli sprouts and live attenuated influenza virus on peripheral blood natural killer cells: A randomized, double-blind study. *PLoS ONE*,2016;11:e0147742.
24. Pattison DJ, Symmons DP, Lunt M, Welch A, Bingham SA, Day NE, *et al.* Dietary beta-cryptoxanthin and inflammatory polyarthritis: Results from a population-based prospective study. *Am J Clin Nutr*, 2005;82:451-455.

25. Reader's Digest. Foods that harm foods that heal. The Reader's Digest Association Inc., 2013.
26. Saif S, Hanif MA, Rehman R, Riaz M, *et al.* Chapter 23 -garlic. In: Hanif MA, Nawaz H, Khan MM, Byrne HJ, eds. Medicinal Plants of South Asia. Elsevier, 2020, 301-315.
27. Stringham NT, Holmes PV, Stringham JM, *et al.* Supplementation with macular carotenoids reduces psychological stress, serum cortisol, and sub-optimal symptoms of physical and emotional health in young adults. *Nutr Neurosci*, 2018:21286-296.
28. Țigu AB, Toma VA, Moț AC, Jurj A, Moldovan CS, Fischer-Fodor E, *et al.* The synergistic antitumor effect of 5-fluorouracil combined with allicin against lung and colorectal carcinoma cells. *Molecules*, 2020:25(8):1947.
29. Tsitsimpikou C, Tsarouhas K, Kioukia-Fougia N, *et al.* Dietary supplementation with tomato-juice in patients with metabolic syndrome: a suggestion to alleviate detrimental clinical factors. *Food Chem Toxicol*, 2014:74:9-13.
30. Venancio VP, Kim H, Sirven MA, Tekwe CD, Honvoh G, Talcott ST, *et al.* Polyphenol-rich mango (*Mangifera indica* L.) ameliorate functional constipation symptoms in humans beyond equivalent amount of fiber. *Mol Nutr Food Res*, 2018:62e:1701034.
31. Wattanathorn J, Somboonporn W, Sungkamanee S, Thukumtee W, Muchimapura S, *et al.* A double-blind placebo-controlled randomized trial evaluating the effect of polyphenol-rich herbal congee on bone turnover markers of the perimenopausal and menopausal women. *Oxid Med Cell Longev*, 2018, 2091872.
32. Welsh EJ, Bara A, Barley E, Cates CJ, *et al.* Caffeine for asthma. *Cochrane Database Syst Rev*, 2010, CD001112.
33. White BC, Lincoln CA, Pearce NW, Reeb R, Vaida C, *et al.* Anxiety and muscle tension as consequences of caffeine withdrawal. *Science*, 1980:209:1547-1548.
34. Yanaka A. Daily intake of broccoli sprouts normalizes bowel habits in human healthy subjects. *J Clin Biochem Nutr*, 2018:62:75-82.
35. Zare E, Alirezaei A, Bakhtiyari M, Mansouri A, *et al.* Evaluating the effect of garlic extract on serum inflammatory markers of peritoneal dialysis patients: A randomized double-blind clinical trial study. *BMC Nephrol*, 2019:20(1):26.
36. Zaynab M, Fatima M, Abbas S, Sharif Y, Umair M, Zafar MH, *et al.* Role of secondary metabolites in plant defense against pathogens. *Microb Pathog*, 2018:124:198-202.