A Comprehensive Review on Antioxidant-Rich Natural Fruit and Vegetable Products and Human Health

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Introduction

Among the various food plants, fruits and vegetables (FAV) are reported to have health-improving benefits. Some FAV such as citrus fruits (orange, grapefruit, lime, lemon), grapes, pomegranates, apples, dates, green and yellow vegetables (peppers), cabbage, strawberries, carrots, dark leafy greens, and banana have been found worldwide to contain antioxidants. A characteristic of antioxidants is that they exert both additive and synergistic effects in reducing the risk of chronic diseases. Fruits and vegetables, therefore, exert protective roles against chronic diseases such as cardiovascular and cerebrovascular, ocular and neurological diseases, strokes, cancer, diabetes, hypertension, and blood-related diseases. Several epidemiological studies have presented compelling evidence that the potential of FAV to combat the majority of these health conditions are associated with the natural compounds found in them. Low intake of FAV was estimated to be responsible for 31% of ischemic heart disease and 11% of stroke worldwide. In the report of the joint FAO/WHO consultation on diet, nutrition, and prevention of chronic diseases, a minimum daily intake of 400–500 g per day of FAV was recommended for the prevention of high blood pressure, stroke, cardiovascular diseases, and other micronutrient related deficiencies. Inadequate intake of FAV is therefore a significant risk-factor that causes several nutritionally related non-communicable diseases (NCDs). The protective effect of FAV has generally been attributed to their antioxidant constituents (natural radical terminators) such as vitamins A, C (ascorbic acid), E (α-tocopherol), β- and α-carotene and glutathione. Alkaloids, terpenoids, sulfur-containing compounds, phenolic and polyphenolic compounds are other antioxidants present in FAV, which reduces oxidative damage by neutralizing the activities of free radicals. These bioactive, non-nutritive plant compounds generally called phytochemicals further engage in the termination of chain reactions by removing the free radical intermediates. Noted that carotenoids, a significant bioactive present in FAV, are particularly effective at inhibiting the oxidation caused by singlet oxygen. Polyphenolic flavonoids, another group of bioactives, are plant metabolites that exert numerous biological and pharmacological properties. Flavonoids consisting of anthocyanins, anthocyanidins, flavonols, flavones, and flavanones have been shown to possess antioxidants, anti-inflammatory, anti-mutagenic, and anticarcinogenic properties. Further reported a synergistic interaction between phenolic acid, β-carotene, and ascorbic acid, as well as between flavonoids and tocopherols inherent in FAV. Fruits and vegetables when consumed separately provide known bioactive that exert beneficial health effects. However, processing which is one of the means of improving the consumption of FAV in combination will further synergistically enhance the effects of bioactives on molecular mechanisms that are important for disease preventions. Combined foods such as salads, ready-to-eat meals, and mixtures of fresh vegetables or fruit ingredients will enhance the synergistic action of the different phytochemicals.

Antioxidants are important ingredients that are present in fruits and vegetables (FAV). With increased consumption of FAV in its raw and processed form, a predominantly plant-based diet rich in FAV could reduce the risk of the development of chronic human diseases. This review highlights the potentials of the various types of antioxidants containing FAV; their impact on human health as nutraceuticals, pharmaceuticals, and phytoceuticals; as well as prospects in tackling some chronic human diseases. The structure and activity relationship of the antioxidant compounds, as well as their mechanism of action, are examined from current scientific investigations. Information provided herein will give more insight into the roles of antioxidant ingredients present in FAV.

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Lichtenthaler and Marx postulated that processed products from FAV, such as juice, are rich sources of bio-accessible antioxidants, though their bioavailability is said to be relatively low. Septembre Malaterre et al. investigated FAV as a source of nutritional compounds and phytochemicals as well as their changes during fermentation. It was observed that though FAV serves as a source of phytochemicals in their raw and unprocessed state, fermentation ensures changes in the forms and profiles of these bioactive, thereby leading to modifications of their health-related properties. This review thus highlights bioactive non-nutrient compounds in FAV in their raw and processed forms, to elucidate their roles in disease prevention and health.

**High antioxidant fruits and vegetables**

Fruits and vegetables are edible plant parts including roots, stalks, tubers, bulbs, leaves, stems, fruits, and flowers. However, the distinct antioxidants that can be derived from FAV include vitamins C and E, carotenoids, and phenolic compounds. Research has further shown that FAV acts as a major source of vitamins, polyphenols, carotenoids, glucosinolates, saponins, and sterols when consumed in sufficient amounts. Some tropical and subtropical fruits such as guava, mango, passion fruit, pineapple, banana, litchi, papaya, passionflower, kiwano, carob, feijoa, star fruit, lime, and longan are utilized as ingredients in the diets of food consumed in North America and Europe. Burton-Freeman et al. stated that consumption of FAV, apart from increasing the antioxidant capacity of the human body, counterbalances the negative effects of high fat and carbohydrate meals. From a taxonomical viewpoint and as shown in the works of Carlsen et al., FAV and its plant parts contain variant levels of bioactive compounds that often result in some FAV recording higher concentration of antioxidants than others. Antioxidants present in FAV include the primary and secondary metabolites of plants. Secondary metabolites constitute most of the antioxidant compounds and they are classified into terpenoids, phenolics, alkaloids, and sulfur-containing compounds based on their chemical structures. Primary metabolites with antioxidant activity include vitamin B complex, protein and nonprotein amino acids, fatty acids, and organic acids. Although substantive information has been provided about the occurrence and content of different chemical compounds in FAV, it is yet to be effectively systemized. The citrus family consists of fruits that are made up of high nutritional and antioxidant properties. Rich in ascorbic acid, citrus fruits also contain flavone glycosides (hesperidin, narirutin, and naringenin), limonoids, flavones (sinensetin and nobiletin), and phenylpropanoids such as hydrocinnamates. Lako et al. investigated the phytochemical flavonols, carotenoids, and the antioxidant properties of a wide selection of Fijian fruit, vegetables, and other readily available foods, showed that green leafy vegetables had the highest antioxidant capacity followed by fruits and root crops. Anyasi et al. also reported that banana ('Muomva-red cultivar') contains a high content of total polyphenols which is an indication that the banana could be a source of bio-nutrients with great medicinal and health functions. A different class of flavonoids has been reported in Opuntia cactus with types and concentrations varying according to variety, tissue type, and maturation. Other reports have indicated that plants in the Cactaceae family produce flavonol 3-O-glycosides (queretin, kaempferol, and isorhamnetin), dihydroflavonols, flavanones, and flavanols. Nearly all reports on flavonoids found in Opuntia cacti have dealt with extraction from the floral tissue.

**High antioxidant-rich fruits**

Fruits with a documented high concentration of antioxidants belong to the plant members of Rosaceae (dogrose, sour cherry, blackberry, strawberry, and raspberry), Empetraceae (crowberry), Ricaceae (blueberry), Grossulariaceae (blackcurrant), Juglandaceae (walnut), Asteraeaceae (sunflowerseed), Punicaceae (pomegranate), and Zingiberaceae (ginger). Pomegranate, grape, orange, plum, pineapple, lemon, date, kiwi, clementine, and grapefruit have been identified with high antioxidant properties. Other fruits associated with a high amount of antioxidants include dog rose, sour cherry, blackberry, strawberry, raspberry, cloudberry, and rowanberry. Among these fruits, berries account for the highest antioxidant content and dog rose has the highest compared to others such as crowberry, wild berry, black currant, sour cherry, wild strawberry, and cowberry. Berries have a high content of phytochemicals such as flavonoids, tannins, stilbenoids, phenolic acids, and lignans.

**High antioxidant-rich vegetables**

Broccoli, brussels sprout, green cabbage, tomato, cauliflower, spinach, leek, lettuce, and sweet pepper have been reported with different antioxidant levels. Hounsome et al. showed that the phytochemical α-carotene and antioxidant β-carotene are richly found in broccoli (1 and 779 mg/100 FW), carrot (4.6 and 8.8 mg/100 FW), tomato (112 and 393 mg/100 FW), pea (19 and 485 mg/100 FW), and sweet pepper (59 mg/100 FW, β-carotene only). These phytochemicals were reported to vary in structure and function from vegetable to vegetable and from cultivar to cultivar, with the level of maturity, postharvest handling, and processing among other factors having a significant impact on their variability. Vegetables rich in ascorbic acid include beans, broccoli, cabbage, cauliflower, cress, pea, spinach, sprouting onion, and sweet peppers. Asparagus, brussels sprout, cabbage, carrot, cauliflower, kale, lettuce, spinach, sweet potato, and turnip are rich sources of vitamin E. Red pepper has also been reported to have a high content of vitamin C (144 mg/100 g). There is an array of evidence that consumption of FAV is important for human health as they are richly endowed with health-improving nutrients. Burton-Freeman postulated that antioxidant-rich FAV increases the antioxidant capacity of the blood, thus decreasing the risk of developing diseases such as cancer, diabetes, coronary atherosclerosis, and gastrointestinal tract diseases. Results from epidemiological and laboratory studies conducted by Eckert, Harding et al., and Rouanet supported the hypothesis that consumption of FAV will prevent and significantly reduce cancer, Alzheimer's diseases, diabetes, and heart diseases. Baskar et al. demonstrated that regularly, free radicals are synthesized in the body either naturally or through external factors such as environmental stress, thus resulting in various degenerative diseases that harm the body. Though the body has an inbuilt defense mechanism to scavenge these radicals, there is a need for the utilization of additional antioxidants available in FAV. Diseases such as cancer, Alzheimer's disease, Parkinson's disease, arthritis, atherosclerosis, and aging are formed in the body as a result of these radicals. Antioxidants especially those synthesized by FAV therefore play a vital role in ensuring that these free radicals are scavenged, thereby preventing them from causing harm. This is especially more important due to the increased...
emphasizes the consumption of antioxidants from natural sources as used for preventive and therapeutic medicine.  

**Vitamin C**  
Bruno et al. stated that the roles of vitamin C include the regulation of cell growth, cell signaling, apoptosis, antioxidants, and as cofactors for enzymes. Vitamin C occurs mainly in FAV and it is reduced by heat during processing; hence, its nutrient density in raw FAV is higher than in processed forms. Vitamin C scavenge reactive oxygen species (ROS) and reactive nitrogen species (RNS) and also regenerates α-tocopherol and coenzyme Q from α-tocopherol and coenzyme Q radical. This resultant action helps in maintaining the antioxidant activities of α-tocopherol and coenzyme Q. The studies by Lee et al. and Chen et al. postulated that ascorbate induces lipid hydroperoxide decomposition to genotoxins in the absence of redox-active metal ions and also leads to a reduction in the growth of aggressive tumor xenografts. As documented in studies conducted on animal species, consumption of FAV rich in vitamin C will greatly help protect the body against cardiovascular diseases, gastrointestinal disorders, cancer, skin infections, and diabetes through the reduction of insulin glycation and an increase in glucose homeostasis.

**Vitamin E**  
Consisting of eight different types: α, β, γ, and δ-tocopherols and the α, β, γ, and δ-tocotrienols, vitamin E can be obtained from vegetable oils, nuts, and seeds of different fruits. Experimental model studies in vitro and in vivo have shown the antioxidant, pro-antioxidative, anti-inflammatory, modulation of cell signaling, antiapoptosis, antiangiogenesis, and apoptosis induction effects of vitamin E. Other works have also shown that α-tocopherol is the major form in human tissues.

Accounting for more than 90% of the literature on vitamin E studies, α-tocopherol is the most studied vitamin E isoflorm, α-tocopherol, and other forms of vitamin E play crucial roles in protection against lipid peroxidation, scavenging of peroxyl radicals, reaction with ROS and RNS and reduction in the synthesis of ROS from NADPH oxidase. The pro-oxidant effect of tocopherol also includes its ability to reduce redox-active metals such as copper and iron. When present in the human skin, vitamin E serves as a vital line of dermal antioxidant protection. Its isomers such as tocopherols and tocotrienols can protect the skin against disease conditions such as dermatitis, UV-irradiation induced skin injury, and chemically induced oxidative stress in animal models. Thus, vitamin E obtained from FAV has found application as cosmetics due to its protective dermal effects.

**Carotenoids**  
Carotenoids consist of a group of lipophilic pigmented compounds that is made up of over six hundred fat-soluble plant pigments. They are chiefly responsible for colors such as yellow, red, and orange present in FAV and from which the compounds are derived. Major carotenoids present in human diets are α-, β-carotene, lutein, lycopene, zeaxanthin, astaxanthin, and β-cryptoxanthin, with these compounds playing an active role in the protection of plants from the damaging and scorching effects of exposure to sunlight. Carotenoids function in the body as a precursor of vitamin A, thus preventing vitamin A deficiency in the body. Carotenoids further undertake antioxidant activities by scavenging reactive species, oxides, and radicals, suppressing inflammatory responses in both in vivo and in vitro systems, as well as assisting in the modulation of cell signaling and induction of apoptosis. This is apart from their roles in cardiovascular protective activities, obesity, cancer, and gastrointestinal disorders.

**Phenolic compounds**  
Stalikas showed that phenolic compounds are secondary metabolites of plant origin that carry one (phenols) or several (polyphenols) hydroxyl moieties in their aromatic ring. Among the major dietary sources are FAV, with an average daily consumption of approximately 1 g/day. Phenolic compounds consist of approximately 8,000 naturally occurring metabolites which are divided into two main groups: flavonoids and non-flavonoids. The flavonoids, a member of the polyphenols, are planar molecules whose varied structure arises partially due to methoxylation, prenylation, glycosylation, or hydroxylation. Their heterocyclic sixmember ring with oxygen is encased by two aromatic rings. Upadhyaya and Parinandi reported that flavonoids are derived from two biosynthetic pathways: the shikimate and the acetyl pathways. Their antioxidant properties are important in protecting plants from oxidative stress. Phenolic compounds are classified as flavones, flavonol, flavan-3-ols, flavones, anthocyanidins, proanthocyanidins, isoflavones, and dihydroflavonols. The flavonoids are derived from various plant sources as used for preventing a plethora of diseases such as heart disease, cancer, and diabetes through the reduction of insulin glycation and an increase in glucose homeostasis.

**Mechanism of action of fruits and vegetable phytochemicals**  
The protective effect of FAV has generally been attributed to their antioxidant constituents (natural radical terminators) from known sources as well as from other unidentified compounds. Niki and Noguchi stated that carotenoids are particularly effective at inhibiting the oxidation caused by singlet oxygen. Gil et al. postulated that flavonoids possess antioxidant properties and antinflammatory, antimutagenic, and anticarcinogenic properties. Antioxidants delay the onset of free radical formation by their ability to donate hydrogen atom (or electron/proton) or chelation of metals involved in the formation of ROS.

Williams and Spencer also postulated that there is a theory emerging evidence that phytochemicals such as flavonoids may play an important role as modulators of intracellular signaling cascades, which are pivotal to the cell machinery. Intracellular signaling cascades are major routes of communication between the plasma membrane and regulatory targets in various intracellular compartments. These signaling cascades seem to consist of up to five tiers of protein kinases that sequentially activate each other by phosphorylation, which consequently affects the activity of transcription factors that regulates gene expression. Jaganath and Crosier showed that the presence of these cascades enables the cells to respond to variant stresses and signals which in turn regulate numerous cell processes, including growth, proliferation, and death (apoptosis). Phytochemicals can exert modulatory effects in cells through selective actions on different components of the signaling cascades. The intracellular concentration of phytochemicals required to affect cell signaling pathways is considerably lower than those required to have an impact on cellular anti-oxidant capacity and their metabolites may still retain the ability to interact with cell signaling proteins, even if their antioxidant activity is diminished. Flavonoids are abundant in plants and the majority of plant tissues possess the ability to synthesize flavonoids. In plants, the leaves,
flowers, and fruits contain flavonoid glycosides; the woody tissue contains aglycone; and the seeds may contain either the flavonoid glycosides or aglycones. Apigenin, a flavone present in parsley and celery hinders proinflammatory cytokines and HIFR, VEGF, and COX-2 expression through the inhibition of nuclear factor-xB (NF-xB), PI3K/Akt, and ATP/cyclic AMP responsive element signaling pathways. 30-106 Tan naringenin, a polymethoxylated flavone that is abundant in peels of citrus fruits serves as an anticarcinogenic agent by suppressing IL-1B-induced COX-2 expression through the inhibition of p38 MAPK, c-Jun N-terminal kinase (JNK), and Akt activation101. Kaempferol, a flavon in broccoli and tea diminishes the activity of inflammation-related genes such as iNOS and COX-2 by blocking signaling of STAT-1, NF-xB, and AP-1 in activated macrophage102 and human endothelial cells103. Quercetin, another flavon present in leafy green vegetables, onions, broccoli, apples, and grapes acts as a potent antioxidant and anti-inflammatory agent. Quercetin inhibits the expression of pro-inflammatory cytokines in mast cells104 and suppresses TNF-induced NF-xB and CPA/p300 recruitment to pro-inflammatory gene promoters105. Furthermore, quercetin diminishes total cholesterol, triglycerides, and low-density lipoprotein and reduces glycemia as well as high-density lipoprotein levels through the inhibition of 11Bhydroxyxysteroid dehydrogenase type 1 106,107. Hamalainen et al. 102 stated that naringenin, a flavanone occurring in oranges inhibits iNOS protein and gene expression by blocking the activation of NF-xB. Naringenin-7-O-glucoside is reported to stop cardiomyocytes from doxorubicin-induced toxicity through the induction of endogenous antioxidant enzymes by phosphorylation of extracellular signal-regulated kinases 1 and 2 (ERK1/2) and nuclear translocation of Nrf2 108 and through the stabilization of the cell membrane as well as the reexpression of antioxidants such as superoxide dismutase109. Cyanidin, an anthocyanidin present in cherries and strawberries was shown to inhibit tumor promoter-induced carcinogenesis and tumor metastasis in vivo through the modulation of the expression of COX-2 and TNF-R110. Cyanidin3-O-rutinoside retards in vivo absorption of carbohydrates through the inhibition of a-glucosidase111. Delphinidin, another anthocyanidin present in dark fruits has been found to contribute antiangiogenic activity through the inhibition of the PDGF-BB/PDGFR receptor (PDGFR)-B in smooth muscle cells112. Anthocyanins suppress lipid peroxidation in caco-2 cells 113 and reduce ethanol-induced migration of breast cancer cells through blocking of ethanolicinduced activation of ErB2/cSrc/FAK pathway essential for cell migration114. Furthermore anthocyanins suppress the proliferation of human breast cancer cell line (MCF-7) by inhibiting 9,10-epoxide-induced cyclooxygenase-2 (COX-2) expression mostly by hindering the activation of the Fyn signaling pathway; 115 prevent nitric oxide synthase and COX-2 and reduction in nitric oxide and prostaglandin E2 production (PGE2);116 as well as inhibit iNOS phosphorylation, thus suppressing NF-xB activity in cell and in vivo models,117-119 thereby contributing to its chemopreventive ability. Carotenoids such as lycopene present in papaya, tomatoes, watermelon, oranges, and pink grapefruit reduce inflammatory response through the lowering of iNOS and COX-2 gene expression 120 as well as IL-12 production through blocking MAPK signaling and the activation of NF-xB in murine dendritic cells. Similarly, ß-carotene inherent in fruits such as carrots, palm fruits, mangoes, papayas, and green leafy vegetables inhibits LPS-induced iNOS, COX-2, and TNF-α expression by decreasing phosphorylation and degradation of iKB and nuclear translocation of NF-xB in macrophages. Lutein, a yellow pigment present in leafy vegetables such as spinach and kale was reported to inhibit LPS- and H2O2induced pro-inflammatory gene expression by decreasing the activity of PI3K and NF-xB inducing kinase (NIK) and phosphorylation of Akt in RAW264.7 cells121-123.

**Fruits and vegetable phytochemicals and cancer**

Cancer, a degenerative disease across the world and one of the leading causes of death, has been associated with lifestyle, environmental and dietary factors. The pathogenesis is attributable to genetic mutation, smoking, heavy metal ingestion, and lack of proper diet. Studies conducted by Lee and Smith and Wolfe et al. have shown that about one-third of all cancer cases and one-half of hypertension and cardiovascular infections are diet-related. However, Willett stated that appropriate dietary intake can prevent more than 30% of cancerous cell growth. Similarly, Amiot and Lairon and Butt and Sultan reported that about 30–40% chances of cancer can be prevented by adopting a proper physical and dietary lifestyle. Consumption of vegetables rich in dietary antioxidants has been linked to a lower risk of different types of cancer, especially the mouth, pharyngeal, esophageal, lung, stomach, and colon cancer.124-130.

**Natural-antioxidant fruit and vegetable products**

Preference for the use of natural products is due largely to their minimal side effects and the increasing preference for natural product used in preventive and therapeutic medicine. There is increasing advocacy and the use of natural vitamins C and E as protection from ultraviolet radiation in the skin and other cosmetic products. Processed food drinks such as fruit juice and wine are presently supplemented with ascorbic acid that is derived from fruits. Natural carotenoid-derived colorants obtained from FAV are increasingly in use to replace artificially synthesized colorants in the manufacture of food products by food processors. Berries and their products are potentially excellent antioxidant sources. However, during the processing of berries to jams, total phenol content is reduced resulting in lower antioxidant values in processed berry products than in fresh berries.131.

**Future direction on natural antioxidant-rich fruits and vegetables**

The health claims, in vitro, from antioxidants present in fruits are still being conducted in experimental models, with many of the claims on their therapeutic effects yet to be verified. Research on phenolic compounds is of growing interest because of the vital biological and pharmacological characteristics which these antioxidants have shown in human health. Hence, bioactive is the topic of discussion at most food and health-related conferences. Further research is therefore needed to verify these health claims and to ascertain antioxidant contents of most pre-packed fresh-cut versus whole FAV, as well as dried FAV that is incorporated into other food products. Recent research revealed that fruit peels and seeds, such as grape seeds and peels, pomegranate peel, wampee peel, and mango seed kernel may potentially possess antioxidant properties. Valorization of the entire plant parts of FAV including peels, rind, seeds, core, rag, stones, pods, vine, skin, pomace, shell, and stem to ensure extraction and utilization of these antioxidants in different food systems are currently ongoing. With the increasing preference and advocacy for natural and minimally processed food products, more studies are ongoing on the antioxidant compounds and their functional, nutraceutical, and prebiotic roles in humans to push forward against cancer, neurodegenerative, and cardiovascular diseases. One of such is the postulation that antioxidant liposomes hold an important role in future research on antioxidants. Genetic engineering has also been suggested as one of the research areas that should aim at breeding genetically modified plants that can produce higher quantities of specific compounds, yielding higher quantities of...
antioxidants. Traditional and exotic fruits as well as ornamental plants are receiving attention more than ever before, all in an attempt to maximize their benefits and significance on human health. Instrumental methods of assessing antioxidant activity are likely to become more important in the future as methods that do not require the use of chemical reagents or solvents reduce waste disposal problems. Thus, different mechanisms of extraction of the antioxidants inherent in FAV aside from the known conventional methods are presently being explored in the food processing industry. These unconventional extraction techniques such as supercritical fluid, pulsed electric field, microwave-assisted, ultrasound-assisted, and enzyme-assisted extraction methods are advantageous due to their high yield, use of organic solvent, low process time, reduced use of energy, and less waste generation.

Conclusion
Though some FAV serves as food mostly in tropical countries, several studies have shown that the consumption of FAV worldwide is insufficient to meet the daily nutritional needs for human health and wellness. With the many health claims attributed to the antioxidant content of FAV, sustained and increased production will lead to increased consumption by humans and an effect of a decrease in degenerative disorders. However, with the increasing world population, there would continually be a reliance on synthetic antioxidant supplements. Therefore, scaling up of production and increased consumption in both scenarios may lead to a reduction of terminal and degenerative diseases.

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