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Review

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# The Science behind Microgreens as an Exciting New Food for the 21st Century

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**ABSTRACT:** Chronic diseases are a major health problem in the United States. Accumulated data suggest that consumption of vegetables can significantly reduce the risk of many chronic diseases. Dietary guidelines for 2015−2020 from the U.S. Department of Agriculture and the U.S. Department of Health and Human Services recommend 1−4 cups of vegetables per day for males and 1−3 cups of vegetables per day for females, depending on their age. However, the average intake of vegetables is below the recommended levels. Microgreens are young vegetable greens. Although they are small, microgreens have delicate textures, distinctive flavors, and various nutrients. In general, microgreens contain greater amounts of nutrients and health-promoting micronutrients than their mature counterparts. Because microgreens are rich in nutrients, smaller amounts may provide similar nutritional effects compared to larger quantities of mature vegetables. However, literature on microgreens remains limited. In this Review, we discuss chemical compositions, growing conditions, and biological efficacies of microgreens. We seek to stimulate interest in further study of microgreens as a promising dietary component for potential use in diet-based disease prevention.

**KEYWORDS:** *microgreens, micronutrients, dietary guidelines, health-promoting, diet-based disease prevention*

## INTRODUCTION

Foods play critical roles in the evolution of human culture.[1] Foods are necessary to sustain human growth, development, and survival by providing calories and essential nutrients.[2] Foods are used to nourish but more importantly have provided a strategy for preventing and alleviating human health problems in various cultures.[3] The contemporary field of food science and nutrition mirrors human evolution, and advances have come about with the injection of information from disciplines such as medicine, biology, and biochemistry. Currently, nutrigenomics and nutrigenetics approaches have been used to advance research in this area.[4] The interest in food and nutrition also evolved from the prevention of deficiencies (vitamins, minerals, etc.) to the prevention of excesses (such as chronic diseases like obesity etc.). The changes in this paradigm are a result of an accumulation of many years of science-based efforts. For example, results from population as well as experimental studies generally support a health protective effect of the consumption of diets that are rich in plant-derived foods.[5] Increased interest in understanding how the microbiome influences an individual's health also has prompted an explosion of work in identifying specific diet−microbiome interactions that lead to health promotion.[6] Although the precise mechanisms remain unclear, consumer interest in health promotion has been the driving force for healthier food (low fat, low calories) with health-promoting functions (e.g., high antioxidant activity, pro-/pre-biotics). It is against this backdrop that new foods such as microgreens have emerged as food sources that may promote health. In this Review, chemical compositions, growing conditions, and biological efficacies of microgreens are discussed. As evidence grows on the biological effects of microgreens, we speculate that these plants may serve as an exciting new food source for promotion of human health.

## WHAT ARE MICROGREENS?

Microgreens are young vegetables (Figure 1A), on average, harvested between 10 and 14 days from seeding. The size of microgreens is between 1 and 3 in. Microgreens are composed of three parts: a central stem, cotyledon leaf or leaves, and a pair of young true leaves (Figure 1C). However, not all young vegetable greens are considered microgreens. Microgreens are smaller than baby greens and harvested later than sprouts. The major difference among sprouts, baby greens, and microgreens is harvest time. Baby greens are generally harvested at 2−4 in. for 15−40 days, while microgreens are harvested right after their youngest leaves appear.[7] In the case of sprouts, the harvest time is earlier than microgreens. Also, sprouts can be differentiated from microgreens by their composition. A sprout consists of seed, root, and stem. On the other hand, microgreens are harvested without the roots. This different growing duration from sprouts or baby greens allows microgreens to develop delicate textures and distinctive flavors. Microgreens are also known for their various colors. Therefore, microgreens are often used for garnishing salads, soups, plates, and sandwiches.

According to the local industry,[8] as early as in the 1980s, chefs in San Francisco, California, began using microgreens. Initially, there were not many varieties offered. Those available

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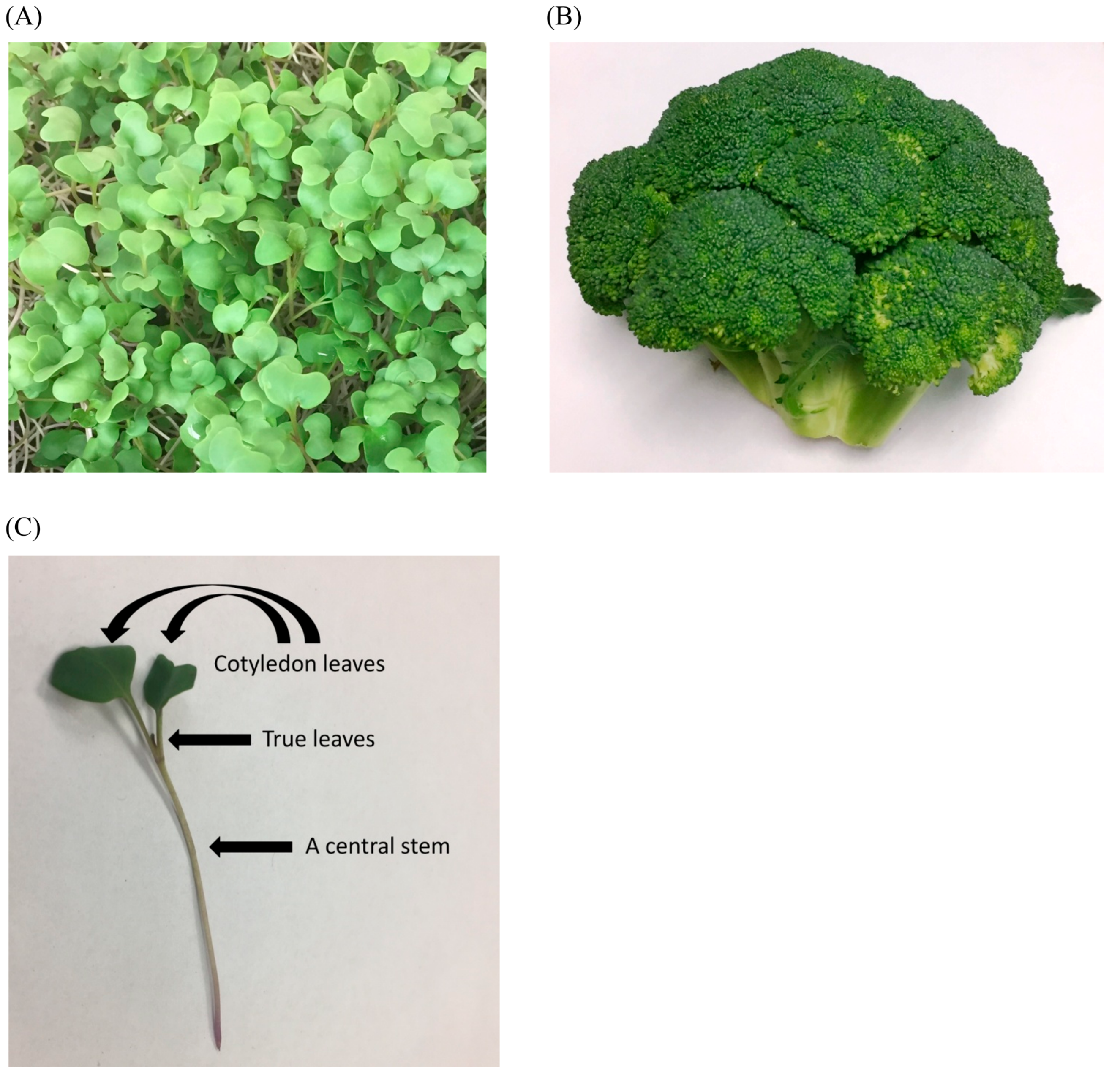


**Figure 1.** Broccoli microgreens and mature counterpart: (A) broccoli microgreens (10 days from seeding), (B) mature broccoli, and (C) the three major parts of broccoli microgreen.

included arugula, basil, beets, kale, and cilantro. However, there are numerous seed companies and growers in the United States that now provide a variety of microgreens. A study reported that there are 25 microgreens that are commercially available[9] (Table 1), with the potential to add value to new food products.

## ■ CHEMICAL COMPOSITIONS OF MICROGREENS (MICROGREEN VS MATURE)

The chemical composition of a microgreen differs considerably from that of the mature form. In this section, the contents of vitamins, carotenoids, total sugars, minerals, glucosinolates, and polyphenols in microgreens will be addressed. The focus is on the 25 plants listed in Table 1, as there is limited information on nutrient content of microgreens.

**Vitamins.** Phylloquinone, also known as vitamin $K_1$, is necessary for blood coagulation and bone remodeling.[10] Usually dark-green vegetables such as spinach, kale, and broccoli are known for their high concentration of phylloquinone. As reported earlier, the 25 varieties of microgreens had a wide range of phylloquinone concentrations from 0.6 to 4.1 μg/g fresh weight (FW).[9] Among the samples, garnet amaranth had the highest concentration of phylloquinone at 4.1 μg/g, and magenta spinach had the lowest phylloquinone content of 0.6 μg/g. In general, green or bright red color microgreens contained greater concentrations of phylloquinone (2.8−4.1 μg/g), and yellow color microgreens had relatively lower concentrations of phylloquinone (0.7−0.9 μg/g). Interestingly, the magenta spinach, which has a similar appearance (e.g., color) to the leading phylloquinone microgreen source garnet amaranth (4.1 μg/g FW), had the lowest


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**Table 1. Twenty-Five Commercially Grown Microgreens[a]**

| commercial name | scientific name | | plant color |
|---|---|---|---|
| | family | genus and species | |
| arugula | Brassicaceae | *Eruca sativa* Mill. | green |
| bull's blood beet | Chenopodiaceae | *Beta vulgaris* L. | reddish-green |
| celery | Apiaceae | *Apium graveolens* L. | green |
| China rose radish | Brassicaceae | *Raphanus sativus* L. | purplish-green |
| cilantro | Apiaceae | *Coriandrum sativum* L. | green |
| garnet amaranth | Amaranthaceae | *Amaranthus hypochondriacus* L. | red |
| golden pea tendrils | Fabaceae | *Pisum sativum* L. | yellow |
| green basil | Lamiaceae | *Ocimum basilicum* L. | green |
| green daikon radish | Brassicaceae | *Raphanus sativus* L.var. *longipinnatus* | green |
| magenta spinach | Chenopodiaceae | *Spinacia oleracea* L. | red |
| mizuna | Brassicaceae | *Brassica rapa* L. ssp. *nipposinica* | green |
| opal basil | Lamiaceae | *Ocimum basilicum* L. | greenish-purple |
| opal radish | Brassicaceae | *Raphanus sativus* L. | greenish-purple |
| pea tendrils | Fabaceae | *Pisum sativum* L. | green |
| peppercress | Brassicaceae | *Lepidium bonariense* L. | green |
| popcorn shoots | Poaceae | *Zea mays* L. | yellow |
| nutrient purple kohlrabi | Brassicaceae | *Brassica oleracea* L. var. *gongylodes* | purplish-green |
| purple mustard | Brassicaceae | *Brassica juncea* (L.) Czern. | purplish-green |
| red beet | Chenopodiaceae | *Beta vulgaris* L. | reddish-green |
| red cabbage | Brassicaceae | *Brassica oleracea* L. var. *capitata* | purplish-green |
| red mustard | Brassicaceae | *Brassica juncea* (L.) Czern. | purplish-green |
| red orach | Chenopodiaceae | *Atriplex hortensis* L. | red |
| red sorrel | Polygonaceae | *Rumex acetosa* L. | reddish-green |
| sorrel | Polygonaceae | *Rumex acetosa* L. | green |
| wasabi | Brassicaceae | *Wasabia japonica* Matsum. | green |

[a]Data from ref 9.

phylloquinone concentration.[9] More importantly, the phylloquinone values for microgreens are relatively high compared to those of mature vegetables. According to the U.S. Department of Agriculture (USDA) National Nutrient Database,[11] mature amaranth, basil, and red cabbage had phylloquinone concentrations of 1.14, 0.41, and 0.04 $\mu$g/g FW, respectively. Comparison of 25 microgreens (Table 1) to the most commonly consumed vegetable in the United States, broccoli, a total of 18 out of the 25 microgreens contain similar or greater phylloquinone concentrations than broccoli's phylloquinone concentration.

Ascorbic acid, also known as vitamin C, is an essential nutrient for human.[12] Total ascorbic acid (TAA), free ascorbic acid (FAA), and dehydroascorbic acid (DAA) were measured in 25 microgreens.[9] The 25 microgreens showed TAA concentrations ranging from 20.4 to 147.0 mg/100 g FW. Among the samples, red cabbage had the highest TAA concentration, and sorrel had the lowest TAA concentration. Compared to mature red cabbage vitamin C concentration from the USDA National Nutrient Database, red cabbage microgreens had 6-fold higher concentration of vitamin C. Also, garnet amaranth (131.6 mg/100 g FW) had a much higher TAA concentration compared to its mature counterpart. Even though some of the microgreens, such as golden pea tendrils and sorrel, had low TAA concentrations, most microgreens had greater TAA concentration than their mature counterparts.[9]

Tocopherols and tocotrienols belong to the vitamin E family, and four isomer forms exist for each tocopherol and tocotrienol: $\alpha$, $\beta$, $\gamma$, and $\delta$.[13] Among the four isomers of tocopherols, the most active vitamin E form is $\alpha$-tocopherol while $\gamma$-tocopherol is the most abundant form found in plants.[14] The green daikon radish had the greatest tocopherol concentrations in both $\alpha$ (87.4 mg/100 g FW) and $\gamma$ (39.4 mg/100 g FW) forms. Also, cilantro, opal radish, and peppercress microgreens showed high concentrations of $\alpha$- and $\gamma$-tocopherols. Even though golden pea tendrils had the lowest tocopherol concentrations of $\alpha$ (4.9 mg/100 g FW) and $\gamma$ (3.9 mg/100 g FW), these values were still higher than the ones from mature spinach leaves (2.0 and 0.2 mg/100 g FW, respectively).[15]

**Carotenoids.** $\beta$-Carotene is a red-orange colored pigment found in fruits and vegetables. $\beta$-Carotene is best known as the precursor of vitamin A and participates in critical physiological roles including vision and development.[16] Due to its structure, $\beta$-carotene can also work as an antioxidant.[17] From 25 microgreens, wide ranges of $\beta$-carotene concentrations were detected. Red sorrel had the greatest $\beta$-carotene concentration of 12.1 mg/100 g FW, and both golden pea tendrils and popcorn shoots had the lowest $\beta$-carotene concentration of 0.6 mg/100 g FW. Cilantro (11.7 mg/100 g FW), the second highest $\beta$-carotene concentration microgreen contained 3-fold more $\beta$-carotene than the mature one. Interestingly, red cabbage microgreen (11.5 mg/100 g FW) had approximately 260-fold more $\beta$-carotene concentration that found in mature red cabbage (0.044 mg/100 g FW). Except for golden pea tendrils and popcorn shoots, most microgreens were rich in $\beta$-carotene. Therefore, microgreens can be considered an excellent source of $\beta$-carotene.

Among seven carotenoids found in the human body, lutein and zeaxanthin are two major carotenoids found in blood.[18] Also, they are the only carotenoids present in the retina and lens of the eye.[19] They function as antioxidants and help protect eyes from UV light.[20] Cilantro had the highest lutein/zeaxanthin concentration of 10.1 mg/100 g FW, and popcorn shoots had the lowest concentration of lutein/zeaxanthin of 1.3 mg/100 g FW. Mature cilantro and red cabbage contain 0.9 and 0.3 mg/100 g FW of lutein/zeaxanthin, respectively.[9] Compared to mature cilantro and red cabbage lutein/zeaxanthin concentrations, cilantro (10.1 mg/100 g FW) and red cabbage (8.6 mg/100 g FW) microgreens had 11.2- and 28.6-fold higher lutein/zeaxanthin concentrations, respectively.

Violaxanthin is a natural carotenoid found in plants.[21] Via function of the xanthophyll cycle, violaxanthin can be converted to zeaxanthin.[22] Among 25 microgreens, cilantro microgreens had the highest violaxanthin concentration of 7.7 mg/100 g FW, and popcorn shoots had the lowest concentration of 0.9 mg/100 g FW. Like other carotenoids, most microgreens tested had high concentrations of violaxanthin.

**Total Sugar Contents.** Total sugar content of six microgreens including bull's blood beet, China rose radish,


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Table 2. Comparison of Selected Phytochemical Concentrations between Brassicaceae Family Microgreens and Their Mature Counterparts

| name | phytochemicals | microgreen | mature vegetable | refs |
| --- | --- | --- | --- | --- |
| red cabbage | total ascorbic acid | 147.0 mg/100 g FW | 24.4 mg/100 g FW | 9, 32, 150 |
| | phylloquinone | 2.8 μg/g FW | 0.04 μg/g FW | |
| | β-carotene | 11.5 mg/100 g FW | 0.044 mg/100 g FW | |
| | anthocyanins | 12.44 μmol/g | 33.36 μmol/g | |
| | glucoraphanin | 4.80 μmol/g dry weight | 0.88 μmol/g dry weight | |
| | glucobrassicin | 1.15 μmol/g dry weight | 1.26 μmol/g dry weight | |
| broccoli | glucoraphanin | 0.67−0.85 μmol/g dry weight[a] | 7.1 ± 2.5 μmol/g dry weight | 32, 151 |
| | glucobrassicin | 10.13−10.81 μmol/g dry weight[b] | 1.1 ± 0.4 μmol/g dry weight | |
| arugula | total ascorbic acid | 45.8 mg/100 g FW | 15.0 mg/100 g FW | 9, USDA National Nutrition Database[c] |
| | phylloquinone | 1.6 μg/g FW | 1.1 μg/g FW | |
| | β-carotene | 7.5 mg/100 g FW | 1.4 mg/100 g FW | |

[a]Harvest day values. [b]Combined values of 1-methoxyglucobrassicin and 4-hydroxyglucobrassicin on harvest day. FW = fresh weight. [c]USDA, Full Report (All Nutrients): 11959, Arugula, raw, National Nutrient Database for Standard Reference Legacy Release, April 2018; https://ndb.nal.usda.gov/ndb/foods/show/3569?n1=%7BQv%3D1%7D&fgcd=&man=&lfacet=&count=&max=&sort=&qlookup=&offset=&format=Full&new=&measureby=&Qv=1&ds=&qt=&qp=&qa=&qn=&q=&ing=.

Dijon mustard, opal basil, peppercress, and red amaranth were compared in an article by Xiao et al.[9] China rose radish had the highest sugar concentration of 10.3 g/kg followed by peppercress, Dijon mustard, bull's blood beet, opal basil, and red amaranth, which had sugar concentrations of 8.8, 7.7, 4.4, 2.0, and 1.7 g/kg, respectively. Compared to microgreens, mature vegetables had higher sugar content. For example, mature peppercress and red amaranth had a sugar concentrations of 44 and 17 g/kg, respectively.[23]

**Minerals.** Minerals are important nutrients for humans, and some minerals are essential nutrients.[24] Recent studies[25,26] suggest that microgreens are excellent sources of minerals. Weber reported that compost-grown broccoli microgreens had between 1.15 and 2.32 times more minerals, including phosphorus, potassium, magnesium, manganese, zinc, iron, calcium, sodium, and copper, than its mature counterpart.[25] Waterland et al. also reported different mineral concentrations of three cultivars of kale at different stages, including microgreen, baby leaf, and mature.[26] According to their studies, dietary mineral concentrations were greater at the early stages of leaf development on a dry weight basis. On a fresh weight basis, a baby leaf contained more minerals than microgreens or mature kale. There was no difference in mineral contents between microgreen and adult kale.

**Polyphenols and Glucosinolates.** The polyphenols and glucosinolates are a wide category of bioactive compounds that have been associated with prevention of several chronic diseases, including cardiovascular disease (CVD), obesity, and cancers.[27,28] Our previous microgreen study compared concentrations of polyphenols and glucosinolates from red cabbage microgreen and mature red cabbage.[29] The study showed that red cabbage microgreen (71.01 μmol/g) had a higher concentration of polyphenols than mature red cabbage (50.58 μmol/g). Also, the glucosinolates concentration was higher in red cabbage microgreen (17.15 μmol/g) than in mature red cabbage (8.30 μmol/g) (Table 2).

In summary, microgreens seem to have greater nutritional values than their mature counterparts based on their fresh weight. However, there are various possible factors, such as cultivars and growing conditions, that can affect the chemical compositions of microgreens. Therefore, further studies are needed to fully document nutrient content of microgreens, as well as how to further enhance their nutritional values.

## GROWING CONDITIONS AND THEIR EFFECTS ON GROWTH AND NUTRIENT CONTENT OF MICROGREENS

In addition to being easy to grow, microgreens are environmental friendly and serve as excellent sources of various nutrients. For example, growing microgreen takes only 10 to 14 days. Also, a study suggests that a broccoli microgreen requires 93−95% less time and 158−236 times less water compared to mature broccoli to have equivalent nutrients. In addition, microgreens do not need fertilizers, pesticides, or energy-demanding transport from farm to table.[25] Growing conditions are important because they directly affect the plant growth and the levels of phytonutrients. In this section, factors that affect the growth of microgreens, including seed sowing rate, fertilizers, and light exposure, are reviewed.

**Seed Sowing Rate.** Seed sowing rate is important for plant growth because it means competition for limited resources such as water and nutrients. Based on the commercial seeding rate of 201 $g/m^2$, Murphy and Pill tested four different sowing rates of 50.25, 100.5, 150.75, and 201 $g/m^2$ using arugula microgreens. They found linear relationships between sowing rate and number of shoots/$m^2$ and shoot fresh weight/$m^2$. However, individual fresh weight/shoot decreased linearly as seeding rate increased. This reflects inter-microgreen competition for resources.[30] Also, a study using beet microgreen reported the same result.[31]

**Fertilizers.** Fertilizers have long been used to supply essential nutrients to plants for their growth. Murphy and Pill reported the effects of different fertilizers on arugula microgreens. As a result, fresh weight per plant or $m^2$ was influenced in the order of calcium nitrate, ammonium nitrate, and urea. In another study, they found these nitrogen sources resulted in greater shoot fresh weight/$m^2$ than ammonium sulfate.[31] Also, Murphy and others reported that using a combination of pre-planting fertilization of the peat-lite mix (soilless growing medium) with calcium nitrate at 2000 mg/L of nitrogen (150 mL/L of medium) with daily post-planting solution fertilization with 150 mg/L of nitrogen led to a great


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Table 3. Selected Microgreen Phytochemicals and Their Potential Protective Roles in Chronic Diseases

| phytochemicals | target chronic diseases | refs |
|---|---|---|
| vitamins ($K_1$, C, E) | inflammation, cancer | 51, 52, 53 |
| carotenoids (β-carotene, lutein, zeaxanthin, and violaxanthin) | inflammation, cancer | 17, 20 |
| polyphenols/flavonoids (quercetin, kaempferol, etc.) | inflammation, CVD, obesity, cancer | 27, 46, 47, 97, 133, 134 |
| glucosinolates (glucoraphanin, glucobrassicin etc.), glucosinolate derivatives (isothiocyanates, I3C, DIM, PEITC) | inflammation, cancer | 67, 68, 69, 70, 71, 72, 73, 74, 88, 119, 120, 121, 122, 123, 124, 125, 126 |
| flavonoids | inflammation, cancer, obesity, type 2 diabetes mellitus | 32, 43, 98, 99, 100, 104, 109 |

yield increase to beet microgreens.[31] In addition, Sun and others reported the potential effect of calcium salt on nutritional value of microgreens using broccoli as a model vegetable.[32] Broccoli microgreens treated with and without calcium chloride differed in glucosinolate concentrations.[32] Surprisingly, calcium treated broccoli microgreens had greater concentrations of glucosinolates than untreated broccoli microgreens, suggesting potential of enhancing nutritional values of microgreens through modulating growing conditions.

**Light Dosage.** The light is a significant influential factor on plant secondary metabolite production.[33] Recent studies suggest that controlling the intensity of light can increase microgreens' nutrients such as carotenoids, tocopherols, glucosinolates, and minerals.[34,35] A study conducted by Kopsell and others tested how light can increase zeaxanthin concentrations in mustard microgreens. For plants, photosynthesis is a necessary tool to maintain energy. Carotenoids are involved in the process of photosynthesis. Carotenoids are pigments integrated in chloroplasts that function as free radical quenchers and dissipate excess thermal energy.[36] For excess energy dissipation, the xanthophyll cycle is necessary, and three carotenoids—zeaxanthin, antheraxanthin, and violaxanthin—are involved in this cycle. When there is an excess of absorbed light, plants use the xanthophyll cycle to transform violaxanthin to zeaxanthin.[37] A study found that exposure to 463 μmol photons/$m^2$/s for a short period of time resulted in a 50% increase of antheraxanthin and a 133% increase of zeaxanthin from mustard microgreens.[34] A similar study using broccoli microgreens and short-duration exposures to blue light found that the blue light led to increases in carotenoids, total glucosinolates, and minerals in broccoli microgreens.[34] In addition, recent studies support the results from these earlier studies. Samuolienė and others tested the effects of blue light on three different microgreens and analyzed the concentrations of carotenoids and tocopherols. They reported that greater blue light intensities had a stronger effect on the accumulation of photosynthetic and carotenoid pigments. However, tocopherols were more sensitive to lower blue light dosage.[38] Taken together, these results have shown that light exposure is a critical factor in altering nutrient profiles in microgreens. Additional research is needed to further investigate the potential effects of light exposure on nutrient accumulation in different microgreens and the molecular biochemical mechanisms involved.

## PREVENTION OF INFLAMMATION AND MODULATION OF IMMUNE PATHWAY BY MICROGREENS

Inflammation plays a central role in the etiology, development, progression of several chronic diseases, including obesity, CVD, and cancers.[39] Hence, the ability to modulate inflammation can have overarching impact on prevention of numerous diseases and management of health care costs. However, inflammation and the immune responses associated with inflammation are complex. We will highlight selected example in the literature to articulate the potential effects of microgreens on inflammation responses regulated by the immune system; these are summarized in Table 3.

As we have reported,[29] consumption of red cabbage microgreen attenuated C-reactive protein (CRP) and tumor necrosis factor alpha (TNF-α) induced in the liver by a high-fat diet. This effect may be due to the microgreen's ability to lower liver lipids, an excess of which has been known to induce inflammatory responses.[29] Additionally, one can also look at some of the prominent inflammation associated pathways to deduce other potential effects that can be induced by microgreens. For example, the nuclear factor kappa light-chain-enhancer of activated B cells (NF-κB) pathway appeared to be central to many inflammatory stimuli. NF-κB plays a critical role in inflammation through its ability to induce transcription of pro-inflammatory genes.[40] Synthesis of pro-inflammatory cytokines, such as TNF-α, interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-8 (IL-8), is mediated by NF-κB.[41] Polyphenols found in various fruits and vegetables have been shown to interfere NF-κB signaling pathways. Initial targets of the interference are the kinases. By inhibiting phosphorylation or ubiquitination of kinases, some polyphenols inhibit NF-κB signaling pathways.[42] Also, inhibition of the interaction of NF-κB subunits with target DNA has been proposed as the potential mechanism for the biological beneficial effects of polyphenols.[43] Both mechanisms can lead to the inhibition of pro-inflammatory cytokines, chemokines, and enzymes regulated by NF-κB. Glucosinolates are natural compounds found in pungent plants as well as cruciferous vegetables.[44] Our red cabbage microgreen study reported that total desulfoglucosinolates concentrations in microgreens (17.15 μmol/g dry weight) were much higher than the mature counterparts (8.30 μmol/g dry weight).[29] Dietary glucosinolates are known to mediate various signaling pathways, and NF-κB is one of the pathways that is affected by glucosinolates. Although a clear mechanism of action is still unknown, it is believed that glucosinolates inhibit catabolism of nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha (IκBα) which inhibits NF-κB activation.[45] Regulation of this critical pathway by bioactive compounds commonly found in microgreens may thus influence immune/inflammatory outcomes. Downstream of NF-κB, cyclooxygenase-2 (COX-2) is one of the major enzymes involved in inducing inflammation. Activation of COX-2 regulates prostaglandin production that can lead to increased and out-of-control inflammatory processes. In recent years, selective COX-2 inhibitors, a type of nonsteroidal anti-inflammatory drug (NSAID), have been developed to treat inflammation. Studies have found that various phytochemicals such as kaempferol, quercetin, and resveratrol may suppress COX-2 activities.[46,47]


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Microgreens contain flavonoids such as kaempferol and quercetin and have a potential to suppress COX-2 activity.

Reactive oxygen species (ROS) are well documented in regulation of cellular pathways, including inflammatory pathways.[48] ROS can elicit multiple effects on NF-$\kappa$B pathways as well as other signaling pathways associated with inflammation.[49] Additionally, inflammation is known to generate reactive oxygen species as defense against pathogens such as bacteria.[48] The ability to regulate ROS would affect multiple aspect of inflammation. Antioxidant effects of food bioactive has been studied extensively.[50] Traditionally recognized nutrients such as vitamin C, E, and K all have been reported to possess antioxidant activities.[51−53] The carotenoids and a wide selection of polyphenols are also well documented to possess antioxidant activities in the literature.[54,55] As mentioned in the section on composition, microgreens are known to be rich in these nutrients and micronutrients. Therefore, microgreens can potentially regulate generation and scavenging of ROS directly and/or indirectly influence ROS-regulated immune responses such as NF-$\kappa$B and other signaling pathways.

Associated with removal of ROS, the NF-E2-related factor 2 (Nrf2)-mediated signaling pathway may indirectly protect cells from inflammatory damage through antioxidant activation.[56,57] Nrf2 coordinates the basal and inducible expression of xenobiotic metabolism-related enzymes (such as antioxidant and phase II detoxification enzymes) to adapt to different oxidative stress.[58] The stability and cellular distribution of Nrf2 are tightly controlled by its inhibitory binding protein Kelch-like ECH-associated protein 1 (Keap1).[59] Through regulation of Keap, Nrf2 accumulates in the nucleus, where it dimerizes with small Maf proteins and binds to the ARE *cis*-regulatory sequences to trigger transcriptional expression.[60,61] A large number of genes have been identified as downstream targets of Nrf2, including NAD(P)H:quinone dehydrogenase 1 (NQO1) and certain glutathione S-transferases (GSTs) (reviewed in ref 62). Nrf2 KO mice, which have lower antioxidant-related enzyme, were reported to result in more severe outcome to lipopolysaccharide (LPS)- or dextran sulfate sodium (DSS)-induced inflammation.[63−65] Nrf2 pathways are known to be regulated by several diet-derived compounds, including those from cruciferous vegetable, such as isothiocyanates and 3,3′-diindolylmethane (DIM).[66] It has been reported that long-term administration of sulforaphane, one of the isothiocyanates, induced antioxidant and phase II drug-metabolizing enzymes in the liver, intestine, skin, prostate, and blood lymphocytes.[67−73] Hence, brassica-derived microgreens which will have considerable amount of these compounds may influence Nrf2 pathway and inflammation.

The arylhydrocarbon receptor (AhR) pathway is also known to be an important transcriptional activator of the xenobiotic pathways, involving critical Phase I enzymes such as CPY1A1, B1 etc.[74] Recent published reports in the literature also support a critical role for the AhR on regulation of the immune system.[75,76] AhR has been shown to affect the transcriptional programs of regulatory (Tregs) and interleukin-17 (IL-17)-producing T helper cells (Th17 cells). AhR has also been shown to participate in the differentiation of FoxP3-IL-10-producing type 1 regulatory T-cells (Tr1 cells) induced by IL-27.[77−79] AhR activation induces the expression of the receptor tyrosine kinase kit and plays a central role in innate lymphoid cell (ILC) development. Moreover, AhR has been shown to modulate the function of the immune system more generally by regulating the function of B cells, dendritic cells, monocytes, and astrocytes.[80−87] Several bioactive compounds were reported to interact with the AhR.[88] Both natural plant food-derived agonists, such as quercetin, resveratrol, and indole-3-carbinol (I3C), and toxic chemicals, such as synthetic polycyclic aromatic hydrocarbons and dioxin-like compounds, are ligands of AhR.[88] Compositional analyses of microgreens show that these plants are rich sources of natural AhR ligands such as quercetin and I3C and have potential to modulate AhR-mediated immune pathways, including regulation of T cells and other immune cells.

Hence, based on the existing literature, we propose a potential role for microgreens in regulation of inflammation-related pathways.

## PREVENTION OF OBESITY, CARDIOVASCULAR DISEASE, AND TYPE 2 DIABETES MELLITUS BY MICROGREENS

Obesity, CVD, and type 2 diabetes are major chronic diseases in the United States, as well as in other parts of the world, and often go hand in hand with consumption of high-calorie, high-fat, and low fruits and vegetables diets.[89] Based on volumes of literature from population as well as experimental studies, consumption of a diet rich in fruit and vegetables is often recommended for prevention of these diseases.[90] Prevention of chronic inflammation, one of the common risk factors for development and progression of these chronic diseases, is a potential mechanism to explain how diet-derived bioactives can act. As described in this Review, many inflammation-related pathways can be modulated by bioactive compounds that are rich in microgreens. Therefore, microgreens may be beneficial for the prevention of obesity, CVD, and diabetes through regulation of inflammation, as summarized in Table 3.

As we previously reported, red cabbage microgreen appeared to prevent high-fat diet induced increase in weight gain.[29] Although the mechanism remains unclear, the effects of this microgreen may be related to an ability to reduce adipogenesis. It has been reported that several phytochemicals found in vegetables/microgreens such as I3C and a metabolite of $\beta$-carotene, retinoic acid (RA), can suppress adipogenesis.[91,92] Choi and others found that I3C directly targets silent mating type information regulation 2 homologue 1 (SIRT1) to inhibit adipocyte differentiation. Activation of SIRT1 has been shown to stimulate various cellular signaling pathways and is involved in thermogenesis regulation, mitochondrial fatty acid oxidation, inhibition of inflammatory cytokines, and glucose uptake.[93−96] Berry and others reported that RA protects mice from diet-induced obesity (DIO) through activating nuclear RA receptors (RARs) and peroxisome proliferator-activated receptor (PPAR) $\beta/\delta$. Also, a number of natural products were shown to inhibit pre-adipocytes proliferation and induce apoptosis.[97] For example, quercetin, one of the most abundant flavonoids present in vegetables, induced apoptosis in 3T3-L1 pre-adipocytes by decreasing mitochondria membrane potential, down-regulating poly(ADP-ribose) polymerase (PARP) and Bcl-2 and activating caspase 3, Bax, and Bak.[97] Also, several other flavonoids, including naringenin, rutin, hesperidin, resveratrol, naringin, and genistein, were also reported to inhibit pre-adipocytes proliferation.[98−100] Hence, microgreen regulation of adipogenesis and lipid metabolisms may exist and thus protect against obesity and obesity-related co-morbidity, including CVD and diabetes.


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Atherosclerosis is one of the major risk factor for CVD.[101] Modulation of the genesis, development, and progression of atherosclerosis has been the main thrust of preventive and therapeutic strategies.[102] Cholesterol metabolism in the liver and efflux of cholesterol from macrophage appeared to play important roles in the development of atherosclerotic plaque.[103] Several polyphenolic compounds, such as the flavonoids, have been reported to regulate cholesterol/lipid metabolisms such as lowering the cholesterol synthesis rate-limiting enzyme HMG-CoA reductase and upregulating LXR and ABCG1 PPAR$\gamma$.[104] The overall effects of these changes would decrease cholesterol synthesis in the liver, promote efflux of cholesterol from macrophages, and inhibit development of atherosclerosis and the likely progression to CVD. Results from our previous study[29] suggest that microgreens may act through lowering of circulating LDL as well as modulating fatty acid metabolisms. This in vivo animal study with microgreens of known chemical compositions demonstrated that modulation of atherosclerosis by dietary microgreens may occur.

An inter-relationship between type 2 diabetes and obesity exists.[105] The risk factors for type 2 diabetes include family history, lifestyle, aging, and obesity.[106] Among these factors, obesity seems to be the most important factor since adult population studies have shown that weight gain significantly increased the risk of type 2 diabetes.[107] Inflammation, through macrophage secretion of TNF-$\alpha$, IL-6, appeared to be the link between development of insulin resistance and obesity.[108] Therefore, microgreens modulation of inflammation may provide protection against insulin resistance. Furthermore, many natural compounds (such as the flavonoids) have been discovered to enhance insulin sensitivity through the PPARs.[109] The PPARs are known to be regulator of lipid metabolisms, adipogenesis, glucose uptake.[110] The metabolic consequence of PPAR activation would increase lipid degradation and glucose utilization.[111] Microgreens are often rich in flavonoids and may act through PPARs to promote insulin sensitivity and protect against type 2 diabetes.

In summary, dietary microgreens may promote health by inhibiting inflammatory pathways associated with the development and progression of obesity, CVD, and type 2 diabetes.

## PREVENTION OF CANCERS BY MICROGREENS

Cancer is the second leading cause of death in the United States.[112] Different from other diseases, the etiology as well as effective treatment remain elusive. Prevention of cancer thus becomes an important aspect of management of the disease. It was estimated that one-third of all cancers can be prevented by a diet that is rich in fruits and vegetables and low in fat and calories.[113] Although mechanisms remain unclear, many diet-derived bioactives have been proposed to have protective effects against various cancers, including the major cancers such as breast, prostate, and colon cancer.[114] Inflammation, again, also may play a significant role in carcinogenesis.[115] The pathways mentioned above are related to inflammation; Keap1/Nrf2, AhR, and NF-$\kappa$B are all involved in carcinogenesis[116−118] and are affected by diet-derived compounds that are rich in microgreens. Acting though inflammatory pathways, microgreens may potentially protect against or prevent cancers. Diet-derived compounds such as I3C and DIM have been reported to activate enzymes involved in xenobiotic metabolism by several groups.[119−121] The ability to activate xenobiotic metabolisms (e.g., AhR and Nrf2 pathways) will allow cells to better defend and clear carcinogens.[58] Microgreens, especially those from brassica vegetable, are rich in precursors of indoles and other inducers of xenobiotic metabolisms.[122] Therefore, activation of Phase I, II xenobiotic metabolizing enzymes may be a potential mechanism by which microgreens protect against cancers. Regulation of sex steroid hormone-mediated pathways may also be a potential way the microgreens can afford protection against hormone-dependent cancers such as breast and prostate cancer. Works from ours as well as several other groups have reported regulation/inhibition of estrogen receptor- and androgen receptor-mediated pathways by diet-derived compounds, including indoles and flavonoids.[123−125] Our previous study showed that I3C and DIM have prostate cancer protective effects.[123] In that study, our group used physiological concentrations of these two compounds and found that cancer protective effects of DIM and I3C are more likely due to their effects on hormone-dependent and xenobiotic metabolisms pathways. Also, mechanistic differences between DIM and I3C were observed from this study. DIM induce both Phase I (CYP1A1) and Phase II (NQO) xenobiotic metabolic enzymes in AhR-dependent fashion. In I3C's case, I3Cs induce Phase I (CYP1A1) enzyme through AhR-dependent fashion but not Phase II (NQO). Even though I3C and DIM showed mechanistic differences, these compounds have similarities that they may act more effectively at earlier stage of prostate carcinogenesis and likely through a combination of effects on steroid hormones and/or xenobiotic metabolism pathway. In addition to our previous study, Meng and others reported that I3C have breast cancer protective effects.[126] The author found that I3C significantly repressed the 17$\beta$-estradiol activated estrogen receptor alpha (ER-$\alpha$) signaling in a dose-dependent manner in breast cancer cell, MCF-7. Also, I3C downregulated expression of the estrogen-responsive genes, trefoil factor 1 (TFF1) and cathepsin-D, and upregulated the tumor suppressor gene, breast cancer 1 (BRCA1).[126] Microgreens may thus modulate breast and prostate cancer progression through regulation/inhibition of sex-steroid hormone-dependent pathways.

Although the complex array of pathways and their interaction with food bioactive that lead to modulation of carcinogenesis remain unclear, there are, as described above and summarized in Table 3, several potential cancer preventive pathways that may be affected by microgreens. These include modulation of xenobiotic metabolisms and inflammation and of initiation, promotion, and progression of cancers. Overall, microgreens may potentially protect against various cancers.

## MICROGREENS AND MODULATION OF THE GUT MICROBIOME

In recent years, a critical role for the gut microbiome in development of chronic diseases, intestinal health, and cancers has emerged.[127−129] The gut microbiome, interfaced between the host and the environment, is now considered to be one of the major component regulating host health and the onset of diseases.[130] Developing ways to manipulate the gut microbiota represents a promising preventive strategy. Diet plays a critical role in modulation of the microbiome, and changes may be rapid.[131] Using bioinformatics tools, Ni et al. reported that >400 compounds present in a plant-based diet are linked to 609 microbial targets in the gut.[132] Flavonoids such as kaempferol, quercetin, apigenin are among the compounds identified in the study. Also, Huang and others reported that quercetin, catechin, and puerarin had activities of regulating


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gut microbiota.[133] Tzounis and others reported high intake of cocoa-derived flavonoids increases the abundance of *bifidobacteria* and *lactobacilli* and reduces the level of plasma triacylglycerol.[134] Phytochemicals can also be transformed by the gut microbiome to metabolites with bioactivity such as anti-inflammatory effects.[135] In addition, bacterial enzyme such as $\beta$-glucuronidase can process phytochemicals to allow uptake by the host and regulate bioavailability and bioefficacy of micronutrients.[136] Microgreens are rich in flavonoids, and therefore it is likely that the gut microbiome can be regulated by consuming microgreen. Furthermore, microbiome processing of the bioactives in microgreen may alter/enhance bioefficacies of microgreens. Hence, it is reasonable to consider modulation of the gut microbiome and consequently protection against a list of diseases associated with microbiome changes. Although interactions of microgreens and the gut microbiome remain unknown, the health consequences may be important and warrant further study.

## ■ MICROGREENS AND REGULATION OF EMERGING BIOLOGICAL PATHWAYS: miRNA, DNA METHYLATION, AND HISTONE MODIFICATION

The field of gene regulation has evolved from transcriptional factors-based regulation to epigenetic-based regulation such as chromatin methylation, histone modification, and regulation through miRNA.[137] Reviews of molecular mechanisms as well as their impact on health of these pathways are well documented in the literature.[138−140] More importantly, diet-derived bioactives have been reported to regulate these pathways in vitro as well as in vivo. Brassica vegetable-derived compounds such as sulforaphane, phenethyl isothiocyanate (PEITC), I3C, and its acid-dimerized derivative DIM were reported to modulate promoter methylation, histone methylation, and regulation of various miRNA.[141] Also, various phytochemicals, including quercetin, curcumin, resveratrol, and lycopene, were found to influence DNA methylation and histone modification.[142] Interestingly, the Keap1/Nrf 2 pathway mentioned above that regulate immune as well as xenobiotic metabolisms pathway appeared to be modulated by food-derived bioactives through epigenetic pathways.[143] Diet-derived bioactives such as curcumin,[144] tocopherols,[145] sulforaphane,[146,147] and DIM[148] were found to modulate DNA methylation and/or histone modification and to restore Nrf2 expression. These effects appeared to correlate with protection against prostate cancer.[149] Hence, microgreens rich in these bioactive phytochemicals (e.g., flavonoids, indoles, and isothicyanates) may regulate miRNA and DNA methylation as well as histone modification and provide protection against inflammation and oxidative stress and prevention of various chronic diseases including cancers.

## ■ SUMMARY AND FUTURE WORK

In conclusion, based on existing literature, microgreens appeared to be excellent low-caloric sources of nutrients and bioactive components.[9] Based on their chemical compositions, we propose that these nutrient-rich plants may provide health-promoting effects related to abilities to prevent the development of the vast array of inflammatory-related chronic diseases. Indeed, microgreens may be a promising new food sources to satisfy interest that consumers have in eating healthy diets. However, several critical questions remain to be addressed: (1) testing and validation of microgreens' health-promoting effects in both animal models and human studies; (2) determining the bioavailability of bioactive components from microgreen; (3) identifying the mechanism of action of microgreen components on cellular pathways in inflammatory processes to also include the microbiome; and (4) determining the optimum growing conditions and post-harvest processing and the effects of these factors on the nutrient content of microgreens. Therefore, further studies are necessary to fully realize the value of microgreens in human health.

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