# Kiwifruit
## *Overview of Potential Health Benefits*

**Keith Singletary, PhD**

Kiwifruit belongs to the genus *Actinidia* (Actinidiaceae) and is derived from a deciduous woody, fruiting vine. It is composed of different species and cultivars that exhibit a variety of characteristics and sensory attributes. Kiwi plants have been grown for centuries in China, where they are known as *mihoutau*. Kiwi plant seeds were brought to New Zealand in the early 20th century, where it was eventually domesticated and sold worldwide. Currently, commercial growth of the fruit has spread to many countries including the United States, Italy, Chile, France, Greece, and Japan. Kiwifruit extracts have been reportedly used in traditional Chinese medicine for relief of symptoms of numerous disorders. In light of growing consumer acceptance of kiwifruits worldwide, there has been an increased attention given to identifying health benefits associated with its consumption. Potential benefits include a rich source of antioxidants, improvement of gastrointestinal laxation, lowering of blood lipid levels, and alleviation of skin disorders. Some individuals report allergic symptoms to kiwifruit, and a considerable research effort is being focused on characterizing kiwifuit's allergenicity among various populations of people. Kiwifruit not only is rich in vitamin C but also is a good source of other nutrients such as folate, potassium, and dietary fiber. This fruit's content of nutrients and biologically active phytochemicals has stimulated investigations into its antioxidant and anti-inflammatory actions that might then help prevent cardiovascular disease, cancer, and other degenerative disorders. Nutr Today. 2012;47(3):133–147

K iwifruit belongs to the genus *Actinidia* (Actinidiaceae) and is derived from a deciduous, woody fruiting vine. It is composed of different species and cultivars that exhibit a variety of physical characteristics and sensory attributes. Kiwi plants were originally grown in mountainous, forested regions of China (as Chinese gooseberry), where it is also known as *mihoutau*.[1,2] Its seeds were

**Keith Singletary, PhD,** is professor emeritus of nutrition in the Department of Food Science and Human Nutrition at the University of Illinois. From 2001 to 2004, he was the director of the Functional Foods for Health Program, an interdisciplinary program between the Chicago and Urbana-Champaign campuses of the University of Illinois. Dr Singletary received bachelor's and master's degrees in microbiology from Michigan State University and his PhD in nutritional sciences from the University of Illinois. Dr Singletary's primary research interests are in molecular carcinogenesis and cancer chemoprevention, specifically identifying and determining the mechanism of action of phytochemicals in fruits, vegetables, and spices as cancer protective agents. He also investigated the biological basis behind the role of alcohol intake in enhancing breast carcinogenesis. He has been recognized with the Senior Faculty Award for Excellence in Research by the College of Agricultural, Consumer, and Environmental Sciences at the University of Illinois and with the Outstanding Graduate Mentor/Advisor award from the Department of Food Science and Human Nutrition. Dr Singletary currently resides in Florida.

Correspondence: Keith Singletary, PhD, University of Illinois, 260 Bevier Hall, 905 S Goodwin Ave, Urbana, IL 61801 (kws@illinois.edu).

brought to New Zealand in the early 20th century, where it was eventually domesticated, renamed, and sold worldwide. Currently, commercial growth of the fruit has spread to many countries including the United States, Italy, Chile, France, Greece, Brazil, and Japan.[3–5]

There are dozens of species comprising the genus *Actinidia*.[6] Although the designation kiwifruit applies mainly to both *Actinidia deliciosa* and *Actinidia chinensis*, the *A deliciosa* Hayward cultivar is the most popular variety marketed commercially. Whereas *A deliciosa* fruit has translucent, green flesh with rows of edible, black seeds covered by a brown, hairy skin, the closely related variant *A chinensis* (Hort 16A) may have yellow flesh that is surrounded by hairless skin. The ZESPRI GOLD kiwifruit cultivar of *A chinensis* has bright yellow flesh, and other variants have been produced with reddish flesh.[3,5] A third unique species *Actinidia arguta* or "hardy kiwifruit" can actually be eaten whole, because it is grape-sized (weighing 5–15g) and is covered by a smooth, hairless, edible skin. Its flavor has been described as more intense, sweet, and aromatic, in part due to its composition of multiple volatile compounds.[7] Like *A arguta*, *Actinidia kolomikta* and *Actinidia polygama* have been developed as frost-resistant varieties and have been grown as ornamental plants in some northern regions.

The chemical composition among kiwifruit cultivars is not uniform and may influence palatability. Whereas the *A deliciosa* and *A chinensis* genotypes have roughly similar sugar content, composed of equal amounts of glucose and fructose and relatively less sucrose, in *A arguta* the ratio of sucrose to glucose and fructose is much higher. Furthermore, *A arguta* has 4- to 6-fold higher levels of myoinositol compared with *A deliciosa* and *A chinensis*, making it one of the richest dietary sources of this sugar alcohol.[3] Myoinositol is a cyclic polyol found in many foods, particularly in fruits. Inositol is an important nutrient for cells within the body. The balance of sugar and organic acids in kiwifruits contributes greatly to their sensory qualities. In this regard, most kiwifruits have citric acid as a predominant organic acid, and, in contrast to other common fruits, the acid-tasting quinic acid predominates as well. Quinic acid is an important metabolite associated with the shikimate pathway in plants.[8] Some kiwifruit constituents may make important contributions to human nutrient requirements.[2] Notably *Actinidia* fruits are exceptionally high in ascorbic acid (vitamin C), although amounts may vary considerably among cultivars. Amounts of vitamin C in the 3 main species generally vary

from 50 to 430 mg/100 g fresh weight,[3,9] with levels in *A chinensis* generally being somewhat higher than in *A deliciosa*, 100 mg and 85 mg/100 g fresh weight, respectively. Kiwifruits are good sources of folate and potassium and contain large amounts of vitamin E in the seed, although the bioavailability of this fat-soluble vitamin may be potentially diminished because of limited human digestibility of the seed. This fruit also contains about 2% to 3% dietary fiber. Sensory acceptance of kiwifruit is also dependent on the presence of calcium oxalate in all varieties, although variation in oxalate content among species has been noted.[10–12] Oxalates can cause oral irritation when certain kiwifruit-derived products are eaten. Depending on the species and cultivar, kiwifruit also contains different pigments including chlorophylls, carotenoids, lutein, and anthocyanins.[2,3,13–16] Free galactose, myosmine, water-soluble vitamins, serotonin, alkaloids, and saponins also have been quantitated in kiwifruit.[2,3,17–22] Moreover, kiwifruit is known to contain appreciable amounts of proteases, principally the cysteine protease actinidin (Act).[3] It should be pointed out that various aspects of kiwifruit cultivation, harvesting, storage, and processing may affect the chemical and nutritional properties of this fruit.[3,14,23–30]

## OVERVIEW OF HEALTH BENEFITS

In ancient China, *Actinidia* plants were used for symptom relief of numerous disorders, such as digestive problems, rheumatism, dyspepsia, and hemorrhoids, as well as a therapy for various cancers.[22] Recently, there has been increased attention given to consumer acceptance of kiwifruits and to potential health benefits associated with their consumption.[21,31–35] The Table provides an overview of some of the potential health benefits of kiwifruit. Examples of various uses for kiwifruit are presented, and an effort is made to give an overview of the variety of scientific research on this topic. Points of view for rating of evidence in each category are based on consideration of cell culture and animal, and human clinical data from the peer-reviewed scientific literature. A rating of *preliminary* indicates that the collective evidence for a specific health benefit is not conclusive in light of the limited and sometimes inconsistent data from animal studies and well-controlled human trials. A rating of *emerging* indicates that data were suggestive of health benefits based on preclinical investigations and some clinical studies. The strength of a potential relationship between kiwifruit and improved health would be improved by additional and consistent reports from larger, well-controlled human studies. A rating of *strong* is reserved for data that are consistent among preclinical and clinical studies, including at least 2 well-designed and conducted human trials. Furthermore, there is substantial evidence of a plausible biological mechanism.

## ISSUES OF KIWIFRUIT SAFETY AND ALLERGENICITY

The allergenicity of kiwifruit constituents has been recognized for over 2 decades. Furthermore, there have been an increasing number of reported kiwifruit allergies as consumption of this fruit continues to expand worldwide.[156,157] In general, the prevalence of kiwifruit allergy needs to be more fully characterized and may differ geographically, with 1 study suggesting that it may be as common as peanut allergy among French school-aged children.[158] It is purported to be among the top 10 food allergy sources based on studies in France, Finland, and Sweden.[159] A recent report suggests that ethnic differences among children may explain some of the variability in incidence of food allergies within populations as well as variations noted in the age at onset of symptoms.[160]

It should be mentioned that, compared with other common food allergies, such as those to tree nuts and peanuts, the allergic response to kiwifruit in general appears to be considerably less severe. The allergic response in adults is often a mild localized oral allergy syndrome that is characterized by oropharyngeal itching and swelling.[161] Nonetheless, systemic reactions are not uncommon, especially in children, and may include anaphylaxis, urticaria, and gastrointestinal (GI) symptoms following kiwifruit intake. Sublingual immunotherapy has been attempted to lessen these symptoms.[156,161–166] Differences in systemic responses to kiwifruits have been documented and, in part, may depend on the species of kiwifruit and on the stability of individual allergen proteins to heating and on their susceptibility to GI digestion. Of interest is the observation that individuals allergic to green kiwifruit demonstrated less severe symptoms following consumption of gold kiwifruit, a difference explained in part to the 50-fold lower content of Act d1 in gold kiwifruit.[158] It is known that the GI digestion of kiwifruit allergens can be affected by other components of food matrices consumed along with kiwifruit.[167–170]

Kiwifruit allergy is often cross-reactive with other allergies, such as that to birch and grass pollen. It also appears to have cross-reactivity to the latex-fruit syndrome.[2,171,172] It should be noted that poor correlations have been reported between suggestive case histories of allergic individuals and in vitro and in vivo diagnostic assays.[161,171,173–175] Considerable research attention is being focused on resolving the reasons for these discrepancies.

Several constituents of kiwifruit have been tentatively identified as allergenic agents. Specifically, 11 kiwifruit allergens have been registered in the Allergen Nomenclature database (www.allergen.org) compiled by the World Health Organization/International Union of Immunological Societies.[159,175] These include the 30-kd cysteine protease Act (Act d1), 24-kd thaumatin-like protein (Act d2), 26-kd cell wall protein kiwellin (Act d5), and cysteine protease inhibitor cystatin (Act d4). However, recent concerns have

| TABLE Potential Health Benefits of Kiwifruit | |
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| **Scientific Evidence for Selected Uses** | **Rating** |
| Antioxidant and anti-inflammatory activities | |
| There is much research interest in identifying dietary antioxidants and anti-inflammatory agents that may retard chronic disease development and other degenerative processes.[36,37] Kiwifruit and its constituents have been the subject of such investigations.[38] | Emerging |
| Preclinical studies | |
| Various *Actinidia* species have been analyzed for their antioxidant chemical profiles.[39–42] For *Actinidia deliciosa* flesh, for example, a chemical analysis identified ascorbic acid and numerous other potential antioxidants. These included σ-tocomonoenol, a vitamin E analog, α-tocopherol, σ-tocopherol, caffeic acid glucosyl derivatives, β-sitosterol, chlorogenic acid, and flavones and flavonones, to name a few.[40,43] The peel also contained appreciable antioxidant phytochemicals, but this has less relevance to typical human kiwifruit consumption and health,[40] unless the fruit is eaten without peeling. The antioxidant capacity of kiwifruit constituents has been measured using various in vitro chemical assays that monitor the quenching, scavenging, or retarding of free-radical generation. For example, compared with other commonly consumed fruits, the total antioxidant capacity of kiwifruit was reported to be less than raspberry, strawberry, orange, and plum, but greater than grapefruit, apple, and pear.[44,45] In in vitro antioxidant assays of several fruit juices including those prepared from orange, grapefruit and apple, kiwifruit juice was determined to be a rich source of potentially antioxidant polyphenols.[46] Furthermore, kiwifruit juice was observed to be a potent inhibitor of lipid oxidation and an effective eliminator of the oxidative stress–inducing agent hydrogen peroxide ($H_2O_2$). The juice also possessed superoxide dismutase–like activity and acted as a copper-reducing agent in vitro.[46] In another report, gold kiwifruits were successively extracted with hexane, acetone, or methanol/water prior to assessment of antioxidant potency.[1] The more hydrophilic fraction of the 70% methanol extract exhibited the greatest superoxide radical-scavenging activity. Within the *Actinidia* genus, the antioxidant capacity and content of total phenols and pigments can vary substantially.[39] For example, frost-resistant species such as *Actinidia arguta*, *Actinidia kolomikta*, and *Actinidia purpurea* were found to have total phenolic, chlorophyll, and carotenoid levels and antioxidant activities that were greater than the commonly consumed *A deliciosa*. A study examining the cellular antioxidant and cytoprotective activities of extracts prepared from 20 genotypes of *Actinidia* germplasm was recently reported.[38] It was observed that hydrophobic components such as carotenoids and some phenolic compounds were effective in inhibiting $H_2O_2$-induced cell death of human HT-29 cells, derived from gastrointestinal (GI) tract cells. Additionally, aqueous extracts from 4 *Actinidia* species demonstrated marked suppression of intracellular peroxyl radical generation in Caco-2 colonic epithelial cells.<br><br>Few animal studies evaluating kiwifruit antioxidant and anti-inflammatory effects have been reported. An extract of *Actinidia polygama* fruit demonstrated anti-inflammatory activity in several animal models,[47,48] an effect in part attributed to inhibition of inducible nitric oxide synthase and cyclooxygenase 2 enzyme expression. In addition, an *A polygama* extract inhibited airway inflammation and hyperresponsiveness in a murine model of asthma.[49] Regarding antioxidant capacity, mice fed kiwifruit juice exhibited lower levels of urinary oxidative stress markers, compared with controls.[50] Cytokine production was also elevated in these mice, which suggests that kiwi juice may have immunopotentiating activity. Feeding of a kiwifruit puree-containing diet to wild-type and Gulo knockout mice was used as a model to determine how the antioxidant ascorbic acid is accumulated by several target tissues.[51] The Gulo knockout mouse lacks gulonolactone oxidase and exhibits a phenotype resembling human vitamin deficiency. This model allowed for time- and tissue-dependent measurement of ascorbate accumulation. After 4 wk, mice fed the kiwifruit-supplemented diet exhibited tissue ascorbate levels that were substantially higher than those for mice consuming an equivalent dose of vitamin C in the drinking water. It was also noted that a suboptimal intake of dietary ascorbate could lead to depletion of intracellular ascorbate, particularly in the liver and kidney.<br><br>This investigation found that kiwifruit is a superior dietary vehicle for delivering this antioxidant vitamin, compared with its supplementation in drinking fluid. The mechanism underlying this enhanced delivery in kiwifruit was not determined. Others have reported contrasting findings on vitamin C bioavailability.[52,53] | |
| Human studies | |
| There is limited epidemiological evidence examining antioxidant benefits of kiwifruit intake. In a population of 96 elderly Japanese, the association between intake of a diet containing kiwifruit and a plasma marker of lipid peroxidation, 8-isoprostaglandin $F_{2\alpha}$ (8-iso-PF$_{2\alpha}$) was determined.[54] Although it is not possible to dissect out the individual contribution of kiwifruit, the collective intake of persimmon, strawberry, and kiwifruit was associated with a significant trend for decreasing plasma 8-iso-PF$_{2\alpha}$, an effect largely attributed to the vitamin C content of these fruits. | |

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| TABLE | Potential Health Benefits of Kiwifruit, continued | |
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| **Scientific Evidence for Selected Uses** | | **Rating** |
| Several studies have been conducted using human subjects to examine whether kiwifruit intake can affect other antioxidant biomarkers. For example, in a study conducted with 10 South Korean males, 150 mL of homogenized kiwifruit flesh was fed to participants.[55] During the subsequent 30 to 120 min, blood samples were collected, and plasma antioxidant capacity was determined in vitro by the 2′,7′-dichlorohydrofluorescein assay. By 60 min after ingestion, the antioxidant action of dietary kiwifruit was maximum (10% decrease in oxidant stress) but was less effective than the antioxidant effects following ingestion of fruit juice prepared from oranges and melons.<br><br>A clinical trial of healthy women also determined that consumption of a meal containing 300 g Hayward kiwifruit was associated with increased postprandial plasma antioxidant capacity.[56] When antioxidant actions were separately characterized as hydrophilic or lipophilic, kiwifruit intake was more effective than eating grapes and strawberries in increasing hydrophilic antioxidant capacity. It did not, however, produce a significant change in lipophilic antioxidant capacity. In a small study involving 3 healthy volunteers, 1 gold or green kiwifruit was eaten 3 times/d for 7 d.[46] Subsequently, oxidative stress markers excreted in the urine, 8-hydroxy-2′-deoxyguanosine (8-OHdG) and N-$\varepsilon$-(hexanoyl)-lysine (HEL), were determined as measures of antioxidant activity toward DNA and lipids, respectively. Intake of gold kiwifruit but not green kiwifruit for 2 to 4 d significantly suppressed levels of the 8-OHdG marker. Intake of both gold and green kiwifruit for 2 to 4 d significantly reduced HEL levels in the urine for all subjects. This relatively stronger action of gold kiwifruit in modulating both oxidative stress markers needs to be confirmed in larger clinical studies in order to better characterize dose and time dependencies of these antioxidant actions. The authors hypothesized that the antioxidant actions of ingested kiwifruit may prevent the development of arteriosclerotic lesions.<br><br>In a randomized crossover study with 14 volunteers, consumption of kiwifruit (1–3/d) for 3 wk led to a significant increase in vitamin C levels in the plasma.[57] Accompanying this increase was a noticeable improvement in antioxidant status as evidenced by the decreased sensitivity of lymphocytes, isolated from the blood of kiwifruit consumers, to oxidative attack by $H_2O_2$ in vitro. Similarly, endogenous oxidation of lymphocyte DNA also was decreased. It should be noted that in this study the magnitude of kiwifruit's effects on oxidative stress was not related to the number of kiwifruit consumed per day. The reasons for this lack of a clear dose response were not determined. In a recent report, 24 healthy volunteers consuming a normal diet were provided either 1 or 2 golden kiwifruits (*Actinidia chinensis*) per day in a crossover study lasting 2 × 4 wk.[58] Plasma vitamin C levels increased after kiwifruit supplementation, and endogenous DNA damage was lowered as measured in samples of circulating lymphocytes isolated from individuals after kiwifruit consumption. Plasma malondialdehyde, a biomarker of lipid oxidation, was not affected by kiwifruit intake. The authors suggested that intake of golden kiwifruit, richer in vitamin C than green kiwifruit, may strengthen resistance against endogenous DNA damage. In contrast, in another study, the short-term intake (single 500-mL dose) of homogenized kiwifruit by 6 volunteers did not affect endogenous DNA damage, although in an ex vivo assay lymphocytes isolated from these kiwifruit consumers were more resistant to oxidative DNA damage induced by $H_2O_2$.[59] Also, male volunteers (n = 27) in another study consumed 3 kiwifruits per day for an 8-wk period.[60] Lymphocytes isolated from the blood were subsequently analyzed for their antioxidant status by assessing their resistance to $H_2O_2$-induced DNA oxidation in vitro. There was no significant effect of kiwifruit consumption on this marker.<br><br>Using a more targeted genomic approach, a recent clinical study of 9 male smokers examined the impact of diets, supplemented with 3 kiwifruits per day, on the expression in blood cells of genes associated with cellular stress defense.[61] Effects were measured using whole-genome microarray technology. It was reported that for groups of men fed either the kiwifruit-supplemented or antioxidant-rich diets, compared with controls, there was significant up-regulation of groups of genes involved in the control of cellular stress defense mechanisms, such as DNA repair, apoptosis, and hypoxia. Likewise, those fed these 2 supplemented diets exhibited an increase in plasma levels of polyphenols and carotenoids, which acted as putative antioxidant biomarkers. The specific phytochemicals and mechanisms responsible for these changes in gene expression were not characterized. The authors suggested that the kiwifruit plant–supplemented diet has the potential to modify stress- and defense-related gene expression and thus could contribute to the prevention of oxidative stress–related degenerative diseases and aging. Such beneficial profiles of gene expression in tissues other than whole blood components in response to kiwifruit intake are not known and would be important information to gather in future clinical trials. | |

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## TABLE  Potential Health Benefits of Kiwifruit, continued

| Scientific Evidence for Selected Uses | Rating |
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| Far fewer studies have evaluated the anti-inflammatory actions of kiwifruit consumption in humans. A cross-sectional analysis of the diet of children with wheezing symptoms observed that intake of kiwifruit was highly protective for wheeze, an effect attributed to its rich vitamin C content.[62] In light of kiwifruit's content of inositol, it is of interest that inositol supplementation has been evaluated for the relief of respiratory distress syndrome in preterm infants.[63] Also a kiwifruit extract–enhanced gluten-free bread was developed to improve sensory and physical attributes of a potential functional food for those with inflammatory bowel disease (IBD).[64]<br><br>Taken together, these data suggest that eating kiwifruit has the potential to inhibit oxidative and inflammatory processes. Collectively, the data supporting antioxidant actions of kiwifruit are more substantial than those related to kiwifruit's potential anti-inflammatory activities. Inconsistencies in antioxidant efficacy of kiwifruit reported in the human studies in part could be due to differences in experimental protocols or kiwifruit species studied. This should be clarified. Dose-response relationships and the length of time of consumption of kiwifruit needed to quantitate an impact on biomarkers of both oxidative stress and inflammation in animal and human studies could be more clearly defined. Confirmation of the consequences of kiwifruit intake also should evaluate the effects of various cultivars and kiwifruit bioactive constituents on other human biomarkers in appropriate patient populations and in healthy individuals at several stages of the life cycle. Despite the potential benefits of antioxidants identified in laboratory, epidemiological, and small human studies, there remain uncertainties, based on findings from prospective clinical trials, as to whether any practical benefit in retarding chronic disease and aging can be expected from dietary antioxidant strategies.[36,37] Nonetheless, better-designed future kiwifruit feeding trials that explore the bioavailability, metabolism, tissue distribution, and biological effects of kiwifruit constituents on relevant disease markers may identify improved strategies for achieving dietary antioxidant and anti-inflammatory health benefits in humans.[36,37] | |
| **GI tract health** | |
| The capacity of dietary factors to improve function of the GI tract has been a topic of considerable research and a target of functional food development.[65] The potential contribution of kiwifruit intake to GI health also has attracted research attention. | Emerging |
| **Preclinical studies** | |
| Two studies examined the capacity of the highly active proteolytic enzyme actinidin from green kiwifruit (*A deliciosa* var Hayward) to improve protein digestion in in vitro models of the GI tract. Using an in-vitro gastric digestion model, an actinidin-containing extract of kiwifruit enhanced the digestion of some, but not all, food proteins compared with samples treated with pepsin alone.[66] Likewise, in an in-vitro small intestine digestion model, actinidin-containing kiwifruit extract was particularly effective in improving the digestion of whey protein, zein, gluten, and gliadin.[67] Apparently related to their proteolytic actions, enzymes from kiwifruit juice were suggested to be responsible for the capacity of this juice to dislodge a meat bolus obstruction in vitro.[68] Cell-based assays have been used to determine whether green and gold kiwifruit extracts could modulate pathways associated with IBD.[69] It was reported that extracts from both types of kiwifruits strongly inhibited the production of the proinflammatory cytokine tumor necrosis factor $\alpha$ (TNF-$\alpha$) from a macrophage cell line stimulated with purified lipopolysaccharide. Moreover, these extracts were able to suppress TNF-$\alpha$ production stimulated by specific ligands of the intracellular receptor NOD2, encoded by a gene that is one of the most common and highest-risk genetic variants in Crohn's disease. Extracts of kiwifruit also have been investigated for their activity toward intestinal epithelial cells isolated from interleukin 10 (IL-10) gene–deficient (IL-10$^{-/-}$) mice,[70] which spontaneously develop colitis. Aqueous and ethyl acetate extracts of both *A chinensis* and *A deliciosa* were tested and found to be effective in suppressing lipopolysaccharide-stimulated activation of cells isolated from both IL-10$^{-/-}$ and wild-type mice. Moreover, the extracts decreased nitric oxide and cytokine secretion, suggesting that further evaluation of the anti-inflammatory action of these extracts in vivo is needed. Collectively, these findings suggest that further testing of kiwifruit to ameliorate IBD is certainly warranted. Recently, a 39-residue peptide, termed kissper, naturally derived from the *A deliciosa* protein kiwellin, was characterized to be a small, anionic cysteine-rich member of a new family of peptides with pH-dependent and voltage-gated pore-forming activity.[71] The authors speculated that kissper likely may affect GI physiology and even have pharmacological use in treating pathologies involving defective ion transport. | |

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| TABLE | Potential Health Benefits of Kiwifruit, continued | |
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| **Scientific Evidence for Selected Uses** | | **Rating** |
| Human studies | | |

Kiwifruit contains about 3.4 g dietary fiber/100 g fresh fruit,[2] which provides about 10% of the recommended daily requirement for dietary fiber. It also has an appreciable amount of the insoluble fiber lignin.[21,72] There is growing evidence that kiwifruit has laxation properties, a potentially important characteristic in light of the increasing proportion of the elderly population in aging societies that experience impaired bowel function.[73] Three reports described changes in bowel function in response to kiwifruit intake. Rush et al[74] provided 38 individuals 1 green, ripe Hayward kiwifruit/30 kg body weight for 3 wk in a study using a crossover experimental design. Intake of kiwifruit was associated with increased frequency of defecation, higher volume of stool produced, and greater softness of bowel motions. In a second study, chronically constipated patients were given 2 green, ripe Hayward kiwifruits per day for 2 wk.[75] For the 33 constipated subjects, kiwifruit consumption significantly increased complete spontaneous bowel motion, improved transit time and rectal sensation, and decreased days of laxative use, compared with controls. No changes in anorectal physiology or bowel symptoms were detected in healthy subjects. The reason for the differences in responses of constipated patients versus healthy controls is not known. In a recent report,[76] the effect of kiwifruit intake on physiological bowel functions in patients diagnosed with irritable bowel syndrome (IBS) was evaluated. Forty-one IBS patients and 16 adults with no IBS were fed 2 ripe Hayward green kiwifruits per day for 4 wk. Kiwifruit consumption of IBS participants significantly increased defecation frequency and decreased colon transit time. As reported by others,[75] no significant effect of kiwifruit on bowel function was noted for healthy adults in this study. The mechanisms underlying the improvement in bowel function demonstrated in these 3 investigations are not well characterized. Furthermore, although the high water-holding capacity and viscous cell wall-water suspensions produced by ripe kiwifruit[77,78] are suspected to be major factors improving laxation by increasing fecal bulk and stool softness, the roles of other kiwi constituents in contributing to the laxative benefits need to be determined. For example, the protease actinidin in a kiwifruit extract Zylax marketed in New Zealand has been promoted as a laxative, although actinidin-specific actions on colonic health have not been substantiated.[2] Additional double-blind, controlled studies in larger, diverse patient populations are warranted to confirm the dose, time, and species dependence of these potentially important properties of kiwifruit, as well as to determine the GI pathologies that kiwifruit intake might improve. It would also be of interest to evaluate whether processed kiwifruit products or beverages might also provide similar benefits for constipated populations and also whether extracted pectic polysaccharides from kiwifruit have similar laxation potency.[2] Furthermore, it has been suggested that there may be individual variation in the ability to digest and ferment plant cell wall constituents, possibly due to differences in gut microflora of subjects.[79] This is an issue that certainly deserves further attention in the context of possible individual variation in laxation responses following kiwifruit consumption.[2] In this regard, a recent investigation by Han et al[80] demonstrated that green kiwifruit intake, apparently due to the fiber content, changed the colonic microbiota in the growing pig model. In particular, kiwifruit-fed pigs evidenced a higher number of total bacteria, *Bacteroides* and *Lactobacillus*, compared with pigs fed control or cellulose-supplemented diets. It would be worthwhile to confirm and expand these in vivo findings in light of the growing recognition that the human microbiome may have a large impact on human health and chronic disease risk.[81,82] It should also be noted that quinic acid present in kiwifruit might have potential GI tract benefit for humans. Specifically, GI tract microflora can metabolize quinic acid to hippuric acid[83] and to tryptophan and nicotinamide.[79] Quinic acid is believed to stimulate antioxidant metabolism.[84] It has been reported that oral administration of quinic acid to 2 healthy volunteers was associated with enhanced DNA repair when evaluated using serum thiol analyses as a surrogate DNA repair estimate.[84] Similar actions of quinic acid were reported in the rat.[85] Whether quinic acid in kiwifruit is present in sufficient quantities to have benefits for human GI physiology and what such benefits might be remain to be determined.[86] Quinic acid is known to be liberated in the small intestine by esterase hydrolysis of quinic acid conjugates present in fruits,[87] which suggests that total quinic acid amounts available to gut microflora may be higher than chemical analyses of free quinic acid might indicate.

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| Cardiovascular health | | |
| Maintaining cardiovascular health has become a major concern for Western societies. Risk factors for cardiovascular disease (CVD) and the metabolic syndrome are interrelated and include dysregulated blood cholesterol levels, blood lipid levels, and blood clotting, as well as development of type 2 diabetes and obesity. Several investigations have evaluated the effect of kiwifruit and its constituents on some of these risk factors. | | Preliminary |

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| TABLE | Potential Health Benefits of Kiwifruit, continued | |
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| **Scientific Evidence for Selected Uses** | | **Rating** |
| Preclinical studies | | |
| Several investigations evaluated the effect of *Actinidia* on processes associated with CVD. In atherosclerotic apolipoprotein E–deficient mice, provision of a fruit extract (prepared from *Crataegus pinnatifida* Bge and *A deliciosa*) for 8 wk resulted in a significant decrease in blood triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) levels, as well as in the LDL-C/total C ratio.[88] Interestingly, the cholesterol-lowering drug, simvastatin, also evaluated in this study, was not as effective as this extract in suppressing plasma TG levels when administered to the mice. Furthermore, in contrast to the extract, no effect of simvastatin on LDL-C levels was observed. In another experiment, mice were orally administered an extract of kiwifruit leaf.[89] This extract suppressed postprandial blood glucose levels in the mice, purportedly due to α-amylase–inhibiting and α-glucosidase–inhibiting activity of the extract. When ursolic acid was isolated from the roots of *A arguta* and administered to rats along with an oral lipid emulsion,[90] the subsequent elevation of plasma TG levels typically following lipid dosing was prevented. Ursolic acid also enhanced lipolysis in adipocytes isolated from these rats. Ursolic acid as well as triterpenes isolated from *A arguta* root showed significant pancreatic lipase inhibitory activity in vitro as well.[91] These studies suggest that ursolic acid may be one constituent contributing to the lipid-lowering effects of *Actinidia* extracts observed in some studies. There is additional preliminary evidence that *Actinidia* can modulate processes involved in the development of diabetes. Specifically, an in vitro evaluation of a methanolic fraction isolated from unripe *A deliciosa* fruit demonstrated activities in 3T3-L1 preadipocyte cells that could have potential benefits against diabetes.[92] For example, this fraction promoted adipocyte differentiation and increased transcription of the gene for the peroxisome proliferator-activated receptor and γ-adiponectin, whereas it decreased mRNA expression for the genes for monocyte chemoattractant protein 1 and interleukin 6. In differentiated 3T3-L1 adipocytes, the fraction also stimulated glucose uptake. In an in-vitro examination of an ethanolic extract from *A arguta* root, several isolated compounds showed significant inhibitory activity toward the formation of advanced glycation end products, a process linked to hyperglycemia and diabetes.[93] In experimental models, administration of inositol, a sugar alcohol present in kiwifruit, was shown to lessen the teratogenic effects of a diabetic environment.[94] Poor inositol status also has been linked to several health conditions including diabetes.[95] | | |
| Human studies | | |
| In a study by Duttaroy and Jorgenson,[96] 30 healthy volunteers were given 2–3 kiwifruits per day for two 28-day periods. Plasma antioxidant and vitamin C levels increased significantly, compared with controls. Platelet-rich plasma samples from the volunteers consuming 2 or 3 kiwifruits per day exhibited a significant decrease in in vitro ADP-induced platelet aggregation, compared with controls. Kiwifruit intake also was associated with a substantial decrease in plasma TG levels, although no impact on total high-density lipoprotein (HDL) or LDL-C was observed. In a later study,[97] however, in which 43 subjects with hyperlipidemia consumed 2 ripe Hayward kiwifruits per day for 8 wk, HDL cholesterol (HDL-C) concentration significantly increased. Although the LDL-C and total C levels measured in this trial did not respond to kiwifruit consumption in this study, the LDL-C/HDL-C ratio and total C/HDL-C ratio significantly decreased. The authors noted that kiwifruit intervention improved blood antioxidant status and lowered markers of lipid peroxidation. In a recent human crossover study (24 subjects) lasting 2 × 4 wk, supplementation of a normal diet with 1 or 2 golden kiwifruits per day decreased fasting plasma TG levels but did not affect plasma levels of total cholesterol, HDL, LDL or glucose.[58] In a crossover trial of 39 healthy subjects, consumption of 1 kiwifruit/30 kg body weight per day for 3 wk had no significant effect on lipid profiles or on glucose and insulin measures.[98] Similar lack of effects was reported for a small study involving 12 healthy volunteers asked to add kiwifruit to their diets at a dose of 1 kiwifruit/30 kg body weight per day for 9 wk.[99] <br><br>Although not evaluated in the context of kiwifruit intake, myoinositol has been suggested to improve insulin sensitivity, lessen diabetes-induced vascular dysfunction, and alleviate the metabolic syndrome.[100] Taken together, these studies provide preliminary evidence that some constituents of kiwifruit plant may be able to counteract specific processes contributing to diabetes, CVD, and possibly obesity. It would be instructive for future clinical investigations to focus on characterization of the effects of kiwifruit dose and length of consumption on blood lipid dynamics, glucose and insulin balance, and on body weight maintenance and energy homeostasis. | | |

*Continues*

| Scientific Evidence for Selected Uses | Rating |
|---|---|
| Dermatological activity | |
| Burn treatment | Preliminary |
| Two recent rat studies demonstrated an intriguing capacity for a dressing prepared from slices of fresh kiwifruit to promote healing of acute burn wounds.[101,102] Specifically, wound surface area was significantly smaller in rats administered kiwifruit dressings, compared with controls, and dry scars detached more rapidly in the kiwifruit-treated group. Additionally, dramatic antibacterial and angiogenic actions of kiwifruit were observed, compared with controls and with a group of rats treated with silver sulfadiazine cream, an antibacterial ointment used in topical burn management.[101] It was noted by the investigators that among the kiwifruit-treated rodents, there were no positive cultures for *Pseudomonas*, *Streptococcus*, or *Staphylococcus*. There were, however, inconsistent results between the 2 studies when the effect of kiwifruit on blood vessel count and inflammation was evaluated. These disparities likely were due to differences in experimental protocols. A suggested mechanism for the improved wound debridement involved the beneficial proteolytic action of actinidin and other degradative enzymes known to be present in kiwifruit. Components responsible for the antimicrobial, angiogenic, and anti-inflammatory actions of the kiwifruit were not determined. Further characterization of this wound-healing effect of kiwifruit dressings is warranted and should include determining what types of wounds exhibit improved healing and whether different approaches to preparation of the kiwifruit-based dressings are effective. The fractions/components of the kiwifruit that are responsible for the various beneficial outcomes need to be identified, and the mechanisms underlying the improved healing need to be clarified. There remains a considerable challenge in translating this wound-healing action of kiwifruit to the practical clinical care of human burn patients. | |
| Treatment of skin disease | |
| Pharmacological uses of extracts from *Actinidia* have been examined for treatment of inflammatory skin diseases. Kiwifruit possesses a heterogeneous mix of water-soluble polysaccharides composed predominantly of neutral galactan and highly acidic arabinorhamnogalacturonans.[77,103] Purified preparations of these polysaccharides from kiwifruit were investigated for their potential use as pharmacological agents in dermatological treatment strategies.[103] These fractions were found to stimulate cell proliferation of human keratinocyte cultures. Furthermore, in an in- vitro 3-dimensional skin equivalent model, these polysaccharides doubled collagen synthesis of fibroblasts. Kiwifruit polysaccharides appeared, therefore, to exhibit potential benefit in modulating skin cell physiology. Kiwifruit extracts have been studied in vivo in several animal studies as agents for the treatment of atopic dermatitis (AD), a chronic inflammatory skin disease. Based on previous evidence that an extract of *A arguta* (PG102) possessed orally active immune-modulating activity in mice,[104] this preparation was subsequently tested as a therapeutic agent for AD.[105] In the NC/Nga murine model of human AD, PG102 extract administration significantly suppressed dermatitis severity and was accompanied by the down-regulation of immunoglobulin E (IgE) and IgG1 and of inflammatory cytokines involved in skin lesion progression. Moreover, epidermis/dermis thickening and dermal infiltration of inflammatory cells were decreased. In another investigation, Kim et al[106] reported similar beneficial effects of an orally administered *A arguta* extract toward chemically induced AD-like skin lesions in NC/Nga mice. The *A arguta* extract also modulated biochemical markers of skin inflammation, an effect that was similar to that of the 2 therapeutic drugs tacrolimus and dexamethasone, although the doses among the 3 treatments were not equivalent. Another isolate from *A arguta* (DA-9102), when administered orally to hairless rats, was reported to substantially suppress AD-like skin lesions in a magnesium deficiency–induced dermatitis model.[107] This beneficial skin response was accompanied by decreased levels of several cellular and biochemical mediators of inflammation. An oral formulation of DA-9102 has been approved for a phase II human trial by Dong-A Phar in Korea. Finally, another extract of *A arguta* (EFF1001) was observed to be effective when used in adjunctive therapy for the treatment of mild to moderate AD in dogs.[108] There is some evidence from a human trial that oral inositol may improve symptoms in patients with psoriasis.[109] Although evidence is accumulating that extracts of kiwifruit have pharmacological use in managing skin disease, it is unclear whether dietary kiwifruit provides a benefit to those with dermatological conditions. | |
| Antimicrobial actions | |
| Extracts and proteins isolated from *A chinensis* and other kiwifruits have been reported to possess inhibitory activity toward a variety of bacterial and fungal agents.[110–114] In contrast, one investigation reported only modest antimicrobial effects of hexane, acetone, or water-methanol fractions of gold kiwifruit. No fractions were active against *Helicobacter pylori*.[1] Two reports observed anti-HIV activity of a methanol fraction isolated from gold kiwifruit.[1,115] In contrast to other plant cysteine proteases, no antihelminthic efficacy of kiwifruit proteases has been observed.[116–118] | Preliminary |

*Continues*

| TABLE | Potential Health Benefits of Kiwifruit, continued | |
|---|---|---|
| **Scientific Evidence for Selected Uses** | | **Rating** |
| Anticancer actions | | |
| There is a substantial amount of in vitro data indicating that kiwifruit extracts or its individual constituents possess antimutagenic or antiproliferative actions that oppose the cancer process. However, supporting information from animal and human clinical studies is limited. | | Preliminary |
| Preclinical studies | | |
| Kiwifruit juice or its extracts were demonstrated to be antimutagenic toward several chemical carcinogens including the heterocyclic amines, such as 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) and the imidazoquinolines (IQ, MeIQ) using several types of in vitro measurement systems.[119–121] Extracts of kiwifruit also suppressed benzo(a)pyrene (BP)-induced mutagenicity[122] and lastogenicity[123] and nitrosamine-induced mutagenicity.[124,125] These actions are relevant to humans, because the heterocyclic amines and the polycyclic aromatic hydrocarbon BP may be produced in foods as a consequence of high-temperature cooking. Nitrosamines can be produced from nitrites and nitrates that are consumed in certain foods such as bacon and cured meats. In contrast, extracts of kiwifruit and other fruits exhibited weak to moderate comutagenic effects, particularly when evaluated at high doses in in vitro assays.[126,127] The physiological relevance of these latter promutagenic in vitro findings is uncertain. Kiwifruit juice was reported to show only a weak effect in inhibiting the activity of human cytochrome P450 3A, an enzyme involved in drug carcinogen and xenobiotic metabolism.[128] Regarding suppression of cancer cell multiplication, extracts and individual isolates from *Actinidia* have been reported to be effective in inhibiting proliferation of several cancer cell lines.[1,128–132] Corosolic acid isolated from *Actinidia valvata* Dunn root effectively induced apoptotic cell death in human cervix adenocarcinoma cells,[131] as did an extract of *Actinidia rufa* root toward SGC 7901 human gastric tumor cells.[132] Extracts of gold and green kiwifruit counteracted $H_2O_2$-induced disruption of gap-junction intercellular communication (GJIC) using WB-F344 rat epithelial stem-like cells.[133] Disruption of GJIC is often observed as normal cells are transformed into cancerous cells. A role for inositol in protection against cancer has also been suggested.[134] In several mouse models, extracts prepared from different portions of several *Actinidia* species have demonstrated antitumor actions.[135–139] For example, polysaccharides isolated from *A chinensis* and *Actinidia eriantha* roots suppressed tumorigenesis in transplantable mouse tumor models.[136,140] This antitumor action in part was associated with enhancement of immune responses. In light of these limited and preliminary findings, it would be worthwhile to evaluate not only the pharmacological efficacy of kiwi plant extracts but also the dietary effect of well-characterized juices or extracts on tumorigenesis in accepted models of spontaneous or chemically induced cancers. | | |
| Human studies | | |
| Kiwifruit extracts have been reportedly used for centuries in traditional Chinese medicine to treat numerous cancers.[1,139] However, documented efficacy and possible mechanisms of action in these human cancer applications remain unknown. Otherwise, kiwifruit uses in the prevention and therapy of human cancer development have not been routinely evaluated. Rather, the impact of kiwifruit on putative human biomarkers of cancer has been investigated. For example, 3 human intervention studies suggest that kiwifruit may protect DNA from damage that could lead to the initiation of neoplasia.[141] In a short-term crossover study, 6 volunteers were given 500 mL of homogenized kiwifruit (equivalent to ~8 fruits). Blood subsequently was collected over a 24-h period, and lymphocytes isolated. Measurement by the comet assay of endogenous DNA damage in isolated lymphocytes showed no difference between the treatment group and the water controls. However, another ex vivo measurement indicated that kiwifruit intake was associated with increased resistance of lymphocyte DNA to $H_2O_2$-induced oxidative damage, compared with controls. In another investigation, 14 volunteers supplemented their diets with 1, 2, or 3 kiwifruits per day for 3 wk in a crossover design study with a 2-wk washout period between doses.[57] Subsequent ex vivo analysis of lymphocyte DNA by the comet assay indicated that kiwifruit intake was associated with a marked decrease in levels of endogenous oxidation of pyrimidines and purines, as well as a substantial increase in DNA repair capacity. An 8-wk intervention trial,[60,141] in which 33 volunteers consumed 3 kiwifruits per day, confirmed that intake of this fruit was associated with a 13% decrease in DNA strand breaks using the comet assay. However, additional, specific evaluation of kiwifruit's effects on nucleotide excision repair and base excision repair capacities yielded inconsistent results. It would be worthwhile to examine the time- and dose-dependent effects of kiwifruit intake on other cancer biomarkers in humans. In light of the content of dietary fiber in kiwifruit and its actions on fecal bulk and transit time, it would be of interest to determine whether this fruit may act as a dietary antimutagen by reducing the fecal content of potential mutagens and carcinogens.[22] | | |

*Continues*

## TABLE Potential Health Benefits of Kiwifruit, continued

| Scientific Evidence for Selected Uses | Rating |
|---|---|
| Miscellaneous effects | Preliminary |

Two publications report that extracts of *Actinidia* species attenuated liver injury induced in rats by carbon tetrachloride.[142,143] This action of one of the extracts was attributed to its oleanolic acid content.[143] There are preliminary findings that kiwifruit extracts have the potential to modulate the immune system. For example, *Actinidia* extracts significantly increased overall immune function in mice[144] and promoted bone marrow cell proliferation in vitro.[145] Catechin isolated from *A arguta* Planch protected mice from myelosuppression induced by 5-fluorouracil.[146] These latter findings suggest that kiwifruit might have benefits in reducing toxic adverse effects of chemotherapeutic agents.[22] Feeding a gold kiwifruit puree to mice improved an antigen-specific immune response, which led the authors to suggest that kiwifruit might be a new type of functional food ingredient.[147] It has been suggested that water-soluble extracts (PG102) prepared from hardy kiwifruit, *A arguta*, may actually have potential use as orally active immune activators for the therapy of allergic diseases.[148,149] In an exploratory clinical trial, an extract of *A arguta* suppressed serum total IgE levels even in asymptomatic subjects with atopy.[150]

Another possible use of kiwifruit was identified when an *A chinensis*–supplemented sports drink was provided to 25 athletes training in hot environments.[151] For those consuming the beverage containing kiwifruit, work time prior to exhaustion was lengthened. Furthermore, the blood volume of kiwifruit-drinking subjects was expanded, blood glucose levels during extended training were maintained, and vitamin C status of study participants was improved, compared with controls. In another human study, a randomized controlled trial of 89 healthy women with low iron stores, consumption of gold kiwifruit along with an iron-fortified breakfast cereal meal improved iron status, compared with controls.[152] In a study of Chinese subjects' consumption of 2 kiwifruits 1 hour before bedtime for 4 wk improved sleep onset, duration, and efficiency in 24 adults with self-reported sleep disturbances.[153] Regarding food uses of kiwifruit constituents, actinidin, in light of its proteolytic capacity, has been used to tenderize meat as well as to improve emulsion stability, texture, and organoleptic properties of sausage products.[154] Kiwifruit phenolics also have been evaluated for their interactions with functional bread components during dough development and bread baking.[155]

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been expressed that some kiwifruit proteins may have been added prematurely to the database without adequate scientific rigor in assessing allergenicity.[175] For example, clinical data substantiating allergenicity may be limited or derived from poorly controlled study populations. Moreover, scientific techniques used among laboratories to identify food allergens may not be appropriately standardized, and inclusion of proteins into the allergen databases may be based only on potentially unreliable in vitro assays.[161,175,176]

It should be noted as well that additional issues may complicate (and may introduce variability in) the accurate assessment of whether kiwifruit may be allergenic and the magnitude of individual responses that may follow ingestion. For example, expression of allergens within fruits may be affected by species, cultivar, ripening stage of the fruit, or postharvest treatment and storage conditions. This information is often not well documented in literature reports.[30,157,161,175,177] The magnitude and patterns of reactivity to kiwifruit allergens may vary because of ethnic/geographical/cultural differences, age of subjects, and other clinical characteristics of those exposed to kiwifruit.[156,158,160,178–180] Lucas and Atkinson[175] have provided a detailed review of unresolved issues regarding kiwifruit allergenicity and have suggested requirements to be met prior to designation of allergens to a database. They also

have posed important questions that the scientific community needs to address in this arena. In light of these reports of kiwifruit allergenicity, of practical interest to food scientists is the finding that industrial heat treatment and homogenization can make consumption safe for children allergic to kiwifruit.[181] Thus, processing may diminish the risk of allergic symptoms in those with allergies to raw kiwifruit.[182]

As mentioned previously, kiwifruit contains oxalate, much of it present as calcium oxalate raphides, which in certain kiwifruit products may cause oral irritation.[2] However, storage of kiwifruit has been reported to diminish oxalate content.[12]

## SUMMARY

It is evident from the scientific literature that kiwifruit has potentially beneficial actions in improving health in several domains. The strongest evidence at this time supports a role for kiwifruit consumption in improving GI tract function, especially in those with constipation or other disorders. Overall, evidence for kiwifruit benefits needs to be expanded through the conduct of well-controlled human trials that utilize larger study populations and that better define the role of kiwifruit dose ingested, the length of kiwifruit consumption needed to obtain meaningful

physiological responses, and any differences due to kiwifruit species or cultivar on biological end points. In that regard, the bioavailability of specific kiwifruit constituents, their subsequent metabolism and tissue distribution, and ultimate biological actions toward specific disease markers can be better characterized in appropriate animal models, and in some cases in humans. Understanding mechanisms of action of kiwifruit and its bioactive constituents in promoting health need to be more fully characterized. Also, determining preparation and processing conditions needed to develop kiwifruit products with demonstrated health benefits and diminished allergenicity as well as discovering new uses for kiwifruit components in novel applications could further expand the already growing markets for consumption of this fruit.[183–185]

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## BURROWES NAMED LONG ISLAND UNIVERSITY PROFESSOR

Congratulations to *Nutrition Today* Editorial Board member, Jerrilynn Burrowes, PhD, to Full Professor at C. W. Post, Long Island University. Burrowes is the chair of the Department of Nutrition and a nationally recognized clinical nutrition leader in the field of kidney disease. Prior to her appointment at C. W. Post, Burrowes was the research coordinator for the Division of Nephrology and Hypertension at Beth Israel Medical Center in New York City, where she was actively involved as an investigator and collaborator on one of the landmark National Institutes of Health–sponsored clinical trials of morbidity and mortality in people receiving maintenance hemodialysis of the past decade, the Hemodialysis (HEMO) Study. She is the author and coauthor of numerous research and review articles published in refereed journals relating to the HEMO Study and other topics. In addition, she is the coeditor of a textbook published by Humana Press in 2008 entitled *Nutrition in Kidney Disease*.

Burrowes's research currently centers on the nutrition assessment and management of adults with stage 5 chronic kidney disease (CKD) who are receiving maintenance dialysis. Dr Burrowes has held many leadership and advisory roles in professional organizations and societies, and she has served on numerous association committees. She has served as a member of the advisory board for the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative and the nutrition work group for the NKF Dialysis Outcomes Quality Initiative, which developed clinical practice guidelines in nutrition for people with CKD. Burrowes is the editor-in-chief of the *Journal of Renal Nutrition*. Congratulations on this well deserved honor!