



## REVIEW ARTICLE

# The Impact of Kiwifruit on Human Health

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## Abstract

The emerging role of diet in the pathogenesis, as well as for treatment, of disease continues to be an evolving area of research. Prevailing literature suggests that the addition of kiwifruit (*Actinidia* species) to the diet may benefit cardiovascular health, immunity, and gastrointestinal function. Kiwifruit's emerging therapeutic value has been implicated in blood pressure management, lipid profile regulation, and glycemic control. Most promising are its implications in digestive health by improving functional gastrointestinal symptoms such as dyspepsia, constipation, and bloating. The synergism of its bioactive constituents such as fiber, vitamin C, phytochemicals, and the enzyme actinidin, likely affect the commensal microbiome to confer these distinctive health benefits, although mechanistic actions need further clarification. Here, we review the proposed mechanistic action of kiwifruit on cardiovascular and gastrointestinal health, although additional clinical studies are needed to further define the role of kiwifruit in promoting health as well as a treatment adjunct for mitigating disease.

## Introduction

The concept of dietary modification to supplement health has existed since the foundations of both Western and Eastern medicine. Hippocrates, often referred to as the father of Western medicine, is attributed as saying, "let food be thy medicine and medicine be thy food," which emphasizes the belief in the role diet plays in health and disease. The earliest description of the kiwifruit, referred to as 'mihoutao,' comes from a poem by Cen Sen during the Tang dynasty (619-907 AD) [1]. Subsequent descriptions of the fruit come mainly from pharmacopeias, Zhenglei bencao (Collected Classified Materia Medica) during the Song dynasty (960-1279 AD) and Bencao Gangmu (Compendium of Materia Medica) from the Ming dynasty (1368-1644 AD) [1]. Kiwifruit (*Actinidia* species) crops are comprised of two main varieties: the *Actinidia deliciosa* 'Hayward,' or green kiwi, and the gold (various *Actinidia* species) kiwi varieties [2]. Kiwifruit are excellent sources of vitamin C, potassium, dietary fiber, antioxidants, phytonutrients, and enzymes [3]. Kiwifruit are also good sources of vitamins E and K, folate, and carotenoids [4]. Research into the health benefits of kiwifruit has focused on the cultivars green kiwifruit and *Actinidia chinensis* 'Hort 16A', ZESPRI® (gold kiwifruit). There has been a growing interest in how the biologically active substances of these cultivars promote health benefits. These health benefits include improvements in metabolic and digestive health, as well as support of immune function. Kiwifruit have also been shown to promote gastrointestinal motility, facilitate digestion, and induce laxation. Additionally, preliminary data links kiwifruit ingestion to favorable changes in the

lipid profile, anti-hypertensive properties, as well as overall decreased cardiovascular risk. The unique combination of fiber, phytochemicals, antioxidants, and the enzyme actinidin, likely act synergistically to achieve these attributable health benefits [3]. Other potential mechanisms through which diet can influence disease have been demonstrated to act via the microbiome. The microbiome potentiates the role diet plays at the intersection of health and disease. However, the nutritional attributes of the kiwifruit and their defined mechanisms remain elusive and require further study.

## Key Nutrients of Kiwifruit and their Health Benefits

### Vitamin C

Due to the lack of L-gulonolactone oxidase, humans are not capable of producing ascorbic acid (vitamin C), making it an essential nutrient [5]. One kiwi weighing 100 gram provides, on average, 80 to 120 mg of vitamin C with ranges from 50 to 430 mg depending on the cultivar [6]. According to the Dietary Guidelines for Americans and the U.S. Department of Agriculture's (USDA) recommendations, for adults, the recommended daily amount for vitamin C is 75 to 90 mg a day for women and men, respectively [7]. Epidemiological studies have indicated that hypovitaminosis C (defined as a plasma

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vitamin C < 23 μmol/L) to be relatively common in the Western world, and vitamin C deficiency (defined as < 11 μmol/L) to be the fourth leading nutrient deficiency in the United States (US) [8]. Plasma saturation has previously been defined as 70 μmol/l with an intake of 200 mg/day [9, 10]. However, one study observed 'optimal' or saturating levels at 60 μmol/l with the same dose (200 mg/d) [11]. It is important to maintain 'optimal' plasma concentrations of vitamin C as it has been demonstrated that sub-saturation levels result in a deficiency in tissue that consequently hinders enzyme function [12].

Vitamin C serves as an important co-factor for many enzymes in a range of biological functions including collagen production, as well as the biosynthesis of L-carnitine, hormones, and neurotransmitters. Ascorbic acid is the most effective antioxidant in human plasma suggesting its major importance for protection against diseases and processes caused by oxidative damage. Studies have also illustrated its utility in improving immune support and function [13].

The bioavailability studies of vitamin C from kiwifruit have determined kiwifruit is an excellent option by which to maintain a steady level of vitamin C in tissue [11, 12]. In patients with hypovitaminosis C, supplementation with half a kiwifruit a day significantly increased plasma vitamin C levels [11]. Two kiwifruit per day achieved plasma saturation, a dose equivalent to a vitamin C intake of 220 mg/day [11]. This finding was corroborated by another study which showed kiwifruit achieved higher plasma levels than a supplement [12]. This suggests the whole food component enhances ascorbic acid delivery [12]. The authors postulated this could be due to the presence of catechin and other flavonoids found in the kiwifruit but no evidence exists of these claims [12].

Furthermore, kiwifruit have been shown to improve iron bioavailability [14, 15]. When added to meals, vitamin C is known to enhance iron absorption [16]. One study evaluated addition of kiwifruit daily for sixteen weeks as a supplement to an iron-fortified cereal in women with low iron stores, and found a statistically significant increase in ferritin levels [16]. This is likely analogous to vitamin C use with iron supplementation given that these form an iron chelate complex which increases iron solubility and facilitates intestinal absorption [16].

### Antioxidants

Antioxidants protect against disease and processes caused by oxidative damage [17]. Oxidation is a chemical reaction that can produce reactive oxygen species (ROS), such as superoxide (O<sub>2</sub><sup>•-</sup>), hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), and hydroxyl radicals (HO<sup>•</sup>) [17]. Excessive ROS leads to oxidative stress, which can damage cells leading to macromolecular changes in lipids, proteins, and DNA [18]. To this point, oxidation is a potential cause of cancer and has been implicated in cardiovascular disease, stroke, respiratory disease, neurodegeneration, and aging [19-26]. A key balancing act exists between antioxidants and ROS for optimal physiological function [17]. Antioxidant defenses are thought to be augmented by dietary antioxidants [17]. Kiwifruit contain several antioxidants, the key of which

is vitamin C. Ascorbic acid is a highly effective water-soluble antioxidant [12]. It acts by scavenging one-electron and two-electron oxidants [12]. Other antioxidant compounds present in kiwifruit include vitamin E (α-tocopherol), carotenoids, polyphenols, chlorophylls, and flavonoids [27]. The antioxidant function of these compounds has been assessed by their radical scavenging of 2,2'-diphenyl-1-picrylhydrazyl radical (DPPH<sup>•</sup>), H<sub>2</sub>O<sub>2</sub>, and O<sub>2</sub><sup>•-</sup> [27].

Evidence is accumulating that kiwifruit contributes to and supports immune function [13]. Several immune benefits have been reported, including improved antioxidant status, enhancement of innate and adaptive immune function, and protection against oxidative stress [13, 28-32]. In one study, the ingestion of 4 kiwifruit daily for 4 weeks reduced severity and duration of selected upper respiratory tract infection symptoms [30]. This improvement was attributed to higher plasma levels of vitamin C. As an antioxidant, vitamin C scavenges ROS which may play a role in the pathogenesis of infections [33]. For instance, it has been reported that during certain viral infections, ROS can suppress helper T cell-dependent immune reactions [33]. It has been reported that ingestion of kiwifruit improves antioxidant status, decreases levels of endogenous oxidation of pyrimidines and purines in DNA, and increases DNA repair mechanisms [34, 35]. Kiwifruit have been shown to protect against lymphocyte DNA oxidation as well when a normal diet was supplemented with either one or two golden kiwifruits per day for 4 weeks [31]. Lymphocyte DNA oxidation is a key biomarker of oxidative damage [31]. This finding signifies the ability of kiwifruit to enhance DNA repair mechanisms [31]. Other studies have demonstrated kiwifruit extract improved gut-associated immune response and modulated markers of both innate and adaptive immunity [29]. Similarly, kiwifruit extract was found to improve immune responses against inflammatory processes associated with inflammatory bowel disease in murine models [36]. These findings suggest that consumption of kiwifruit may thwart oxidative stress although further study and human trials are warranted.

### Fiber

According to the Institute of Medicine, the recommended daily fiber intake for adults is 25 gram for women and 38 gram for men [37]. However, average fiber intake for US children and adults are less than half of the recommended levels [38]. Kiwifruit is known to contain approximately 2% to 3% dietary fiber comprised of one-third soluble fiber and two thirds insoluble fiber [39]. The soluble fiber fraction contains almost exclusively pectic polysaccharides, whereas the insoluble fiber is mostly cellulose and hemicelluloses [40]. The health benefits of fiber intake include significantly lowering the risk for developing coronary heart disease, stroke, hypertension, diabetes, obesity, and colorectal cancer [41]. A meta-analysis of observational and clinical studies reported significantly lower bodyweight, systolic blood pressure, and total cholesterol when daily intake of dietary fiber was between 25 gram and 29 gram [41]. Dietary fiber benefits several gastrointestinal disorders

such as irritable bowel syndrome, constipation, and stress-induced gastrointestinal symptoms [42-45]. Fiber modulates metabolism by reducing the transit time of carcinogens in the lumen as well as decreasing the digestion and absorption of nutrients [45]. In particular, the symptoms of functional gastrointestinal disorders, which include chronic nonspecific diarrhea and functional constipation, have been shown to be ameliorated by fiber as dietary soluble fiber improves gut homeostasis via production of short-chain fatty acids (SCFAs) [46]. SCFAs are the main bacterial fermentation products of dietary fiber. SCFAs have been associated with beneficial effects on immunity, enhanced motility, absorption, and changes in the commensal microbiome [47-54].

One of the physiological benefits of fiber arises from the organic acid by-products of bacterial fermentation of the soluble fiber. SCFAs include acetate, propionate, butyrate, valerate, and caproate [55]. SCFAs have anti-inflammatory effects which contribute to optimal intestinal function via local signaling pathways [55, 56]. In the duodenum, SCFAs enhance mucosal defense mechanisms via serotonin (5-HT) and glucagon-like peptide (GLP) signaling [55]. SCFAs also act through G-protein coupled receptors located in the intestine and elsewhere throughout the organism [47, 48]. These pathways improve host immunity through various mechanisms: secretion of immunoglobulins, induction of regulatory T-cell tissue repair, antimicrobial peptides, and mucus production [47, 57]. These effects optimize intestinal function and barrier integrity [50, 57]. SCFAs have also been shown to increase human  $\beta$ -defensin 1 and 2 (HBD-1 and 2) production by epithelial cells [52]. Human  $\beta$ -defensins are antimicrobial peptides, an important component of the innate immune system [58]. In one study the fermentation products of in vitro digestion of kiwifruit significantly up-regulated HBD-1 and 2 production in colonic epithelial cells [52]. The increase in SCFAs secondary to kiwi ingestion was corroborated by another in vitro study that sought to examine microbiome changes in response to kiwi ingestion [53]. The study showcased an increase in commensal microbes secondary to the kiwifruit fermentation products. Together, this suggests kiwifruit enhances innate immunity via SCFA production by affecting the commensal intestinal microbiome. In summary, the anti-inflammatory properties of fiber act through various local signaling pathways to maintain mucosal integrity, minimize pro-inflammatory cytokine cascades, enhance mucosal defenses, and beneficially modulate the commensal microbiome. Consequently, a lack of fiber may compromise intestinal barrier function via catabolism of the mucous layer, increased permeability, and increased bacterial contact.

### Actinidin

Kiwifruit protein content is comprised predominantly by the enzyme actinidin and its inactive forms, thaumatococin-like protein, kiwellin, and kirola [59]. Actinidin comprises up to 40% of soluble proteins in green kiwifruit but less than 1% in gold cultivars [60]. Actinidin is a protease and when active can play a role in aiding the digestive process with the potential

to influence protein digestion [61]. There have been both in vitro and in vivo studies on the effect of actinidin from green kiwifruit extracts on gastric digestion and gastric emptying in a range of dietary proteins [60-65]. Collectively, these studies showed the presence of actinidin enhanced the digestion of dietary protein. For instance, one in vitro study examined the effect of actinidin extracts from green kiwifruit on digestion of dietary protein (soy, meat, milk, and cereals) under simulated gastric conditions [63]. The addition of actinidin extract enhanced the digestion of whey protein, zein, gluten, and gliadin by up to 48%. Another study aimed to measure protein digestion utilizing both gastric and duodenal digestion parameters with and without actinidin [64]. Results indicated actinidin enhanced gastric digestion of proteins especially when pepsin and acid secretions were insufficient as may be the case in those with compromised gastric function. In addition, two in vivo studies using murine and swine models demonstrated that the addition of actinidin enhanced gastric digestion and emptying of beef muscle proteins [60-65]. This implies actinidin may serve as a therapeutic tool in those with delayed gastric emptying, impaired gastric digestion, or those with symptoms of functional gastrointestinal disorders as it is discussed in the gastrointestinal health section.

## Clinical Applications of Kiwifruit

### Glycemic Control

The glycemic index (GI) of a particular food provides an estimate of the relative blood glucose raising ability due to the amount of carbohydrate. Green and gold kiwifruit have been determined to be of low GI with clinically measured glycemic indices of 39 and 48, respectively [66]. Glycemic response to a fruit depends not only on the glycemic indices, but also on the amount of carbohydrate in the fruit as well as the non-sugar components. Foods with a low GI produce lower postprandial blood sugar levels and a lower overall blood sugar response than do foods with a high GI [67]. Kiwifruit contains only about 12% of available carbohydrate and a low GI; thus the synergistic combination of the two components ensures the fruit to be a suitable option for those with glucose intolerance [68]. These observations are important for those with diabetes as both postprandial and chronic elevated blood glucose concentrations have direct and indirect effects on disease progression and contribute to obesity [67].

The low GI value of kiwifruit has been observed in both healthy human subjects and those with type 2 diabetes [68]. Several studies demonstrating the effect of kiwifruit consumption on glycemic response have been conducted. Two animal studies using murine models of healthy and diabetic subjects demonstrated *A. deliciosa* fruit extract decreased blood glucose levels significantly compared to diabetic control group [69, 70]. Another in vivo study evaluated the addition of two kiwifruit daily and found a statistically significant decrease in glycemic response and improved glucose homeostasis [70]. This glycemic lowering effect was observed with co-ingested carbohydrates on an equal carbohydrate basis thus suggesting another component mechanistically. It has been postulated that

the glycemic response is due to the synergistic effect of the dietary fiber, actinidin, phytochemicals, and the fruit acidity combined with the buffering capacity of its organic acids [40]. Further, SCFAs also have been indicated in glycemic response and further exploration of this effect has been investigated [49]. SCFAs increase GLP, incretin hormones that act to lower serum glucose [55]. One study investigated the effect of vinegar supplementation on glycemic response and found an inverse relationship between acetic acid and glucose and insulin responses [72]. Together, these findings indicate the emerging therapeutic value kiwifruit can have in improving glucose tolerance.

### Lipid Regulation

Dietary consumption of fruits and vegetables is associated with decreased cardiovascular risk. One thought is that this is in part due to better control of hyperlipidemia as a modifiable risk factor for cardiovascular disease. Kiwifruit have been implicated to modify serum cholesterol levels to a more favorable profile through decrease in total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) with increase in high-density lipoprotein (HDL) [73–75].

One study evaluated supplementation of two kiwifruit daily for eight weeks and found a statistically significant increase in HDL by 0.14mmol/L (5.4mg/dL) and correspondingly significant decreases in the LDL/HDL ratio by 0.31 as well as the TG/HDL ratio by 0.43, all of which are associated with cardiovascular benefit [73]. Another study evaluating healthy patients supplemented with two green kiwifruits daily for four weeks found a statistically significant increase in HDL by 0.04mmol/L (1.5mg/dL) and decrease in the TC/HDL ratio by 0.15 [74]. A third study supplemented two or three kiwifruits daily for 28 days and demonstrated a statistically significant decrease in TG by 0.29mmol/L (26mg/dL) and 0.35mmol/L (31mg/dL) with consumption of two versus three kiwi fruit, respectively [75]. Though, these findings contrasted with a study that found no change in any lipid profile components over a nine-week period with kiwifruit supplementation [76]. A meta-analysis evaluating lipid alteration following kiwifruit supplementation did not yield a statistically significant change in lipid profile, though the changes trended favorably [77]. This analysis found decreases in TC by 0.15mmol/L (5.8mg/dL), TG by 0.23mmol/L (20mg/dL), and LDL by 0.41mmol/L (16mg/dL) as well as an increase in HDL by 0.15mmol/L (5.8mg/dL), though none were significant. These studies showcase conflicting, but generally favorable, effects on serum lipid profiles.

There are multiple physiologic explanations for this proposed effect. One study of kiwifruit extract found inhibition of HMG-CoA reductase in the cholesterol synthesis pathway [78]. Additionally, consumption has been linked to decreased LDL oxidation, another cardioprotective effect [73]. Volunteer studies have illustrated decreased platelet aggregation, and in vitro studies have also demonstrated increased fibrinolysis, both of which contribute to decreased clot formation and propagation [75, 78, 79]. Finally, the fiber component of

kiwifruit acts as a prokinetic, and this can contribute to decreased cholesterol reabsorption and consequently lower serum lipids [73].

### Blood Pressure Management

Intake of kiwifruit has been shown to have an antihypertensive effect. Both in vitro and human studies with kiwifruit extract and dietary addition of kiwifruit have shown a decrease in angiotensin-converting enzyme (ACE) activity [78, 79]. This effect is presumed to be the means by which kiwifruit exerts blood pressure control due to the inhibition of the renin-angiotensin-aldosterone system. Although, the underlying mechanism for ACE inhibition by kiwifruit is still unclear.

The clinical studies evaluating the effect of kiwifruit on blood pressure suggest a favorable impact. One study evaluated kiwifruit versus a high antioxidant diet versus a control group in a hypertensive male-smoker population on an average of three antihypertensive agents [79]. Consumption of three kiwifruits daily over eight weeks was associated with a statistically significant decrease in both systolic and diastolic blood pressures of 10 mmHg and 9 mmHg, respectively [79]. This contrasted with a statistically significant reduction of only systolic blood pressure by 10mmHg in hypertensive patients in the high antioxidant diet group, while there was no significant change in blood pressure within the control group. Another study expanded the study population and compared blood pressure reduction in stage I hypertensive patients who were assigned to supplement diets with three kiwifruits versus one apple daily [80]. Apples supplementation was chosen as a control arm due to lower potassium and antioxidant (measured by Ferric-reducing antioxidant power) compared to kiwi fruit [80]. This study demonstrated decreases of 3.6 mmHg and 1.9 mmHg in systolic and diastolic blood pressures, respectively, when compared to the apple group. A subsequent meta-analysis of five randomized-controlled trials found a decrease in systolic pressure by 1.72mmHg and diastolic blood pressure by 2.35mmHg, that were not statistically significant [80].

### Gastrointestinal Health

The strongest evidence for the health benefits of kiwifruit exist in its effect on digestive health. As mentioned in the introduction, Western and Eastern medicine culminate at the crossroads of diet in health and disease, and what better intersection point than the gut. Hippocrates is also attributed to saying, “all disease begins in the gut.” The previously mentioned pharmacopeias also reference medicinal usage of kiwifruit for treatment of digestive symptoms including indigestion, vomiting, and GI irritability [3]. Recent clinical evidence corroborates that kiwifruit improves functional gastrointestinal symptoms such as constipation, functional gastrointestinal disorders, and irritable bowel syndrome.

### Constipation

Kiwifruit have been shown to relieve constipation in several clinical trials [81-83]. The laxative effect of kiwifruit has been attributed to its fiber content, which is approximately 2-3%

of its dry weight. As described earlier, the fiber content of kiwifruit is approximately two-thirds insoluble and one third soluble fiber [39]. These components and their associated physicochemical properties likely act in concert with actinidin which aids protein digestion, and other phytochemicals in order to induce laxation.

One of the physiological benefits of fiber arises from bacterial fermentation of soluble fiber to produce SCFAs [49]. SCFAs enhance water and electrolyte absorption, modulate mucosal growth, maintain epithelial-microbial barrier function, and is thought to stimulate colonic motility [84, 85]. Although there have been several theories on the potential underlying prokinetic effect of SCFAs, studies have shown conflicting results [85-89]. In murine models, propionate induced phasic contractions in the proximal, middle and distal segments of the rat colon [86]. However, in other murine studies this effect was not observed [85, 87]. Conversely, in guinea pig models, the effect on frequency of full-length propagations, short propagations, and non-propagating contractions was dependent on the nature of the SCFA and chain length [88]. Further, a more recent study reported that SCFAs significantly stimulated fecal pellet propulsion via an intraluminal endogenous 5-HT mechanism [90]. The differing conclusions may be attributed to the different animal models or experimental methods, such as the nature and form of SCFA used. Although the exact role of how SCFAs modulate motility has not been elucidated, several mechanisms for the effect of SCFAs on gut motility have been investigated and include an enteric reflex involving sensory neurons and their intermediaries, mucosal 5-HT signaling, a neuroendocrine mechanism involving PYY, and a direct action on colonic smooth muscle [85, 89, 90].

Another of the physiological benefits of fiber arise from the physicochemical properties of any fiber that remains unfermented. The insoluble and soluble fiber component of kiwifruit contains hydration properties in the gut that impacts stool bulk and bowel habits [91]. These hydration properties include: swelling, water retention capacity, and viscosity [92]. Insoluble fiber stimulates water secretion promoting improved stool transit time [91, 92]. Additionally, the high water retention capacity of soluble fiber increases stool water content [91]. The pulp of the kiwifruit, which is mostly comprised of insoluble cellulose fibers, possesses large water retention capacity, calculated to be 12-13 gram of water per gram of insoluble fiber [40]. Water retention capacity is the amount of water per gram that is bound to the insoluble fiber. This is important clinically as it hydrates the stool, increasing its bulk and volume, which in turn decreases stool transit time [93]. Additionally, the presence of non-soluble fiber contributes to the osmotic bulking facilitating stool transit. The effect of kiwifruit on constipation and motility may be a result of a combination of fiber content with high water absorptive capacity acting as a stool bulking agent as well as SCFAs and other phytochemicals which may stimulate motility [51]. It has been proposed that actinidin may also affect motility, acting on prokinetic colonic receptors via an unknown mechanism [94].

Kiwifruit as a digestive aid has been studied clinically and been shown to improve parameters of laxation, including frequency and ease of defecation, stool bulk, and softness. It has been demonstrated that consumption is also associated with increased stool frequency in healthy volunteers as well as elderly patients [51, 95]. This is corroborated by imaging data showing an increase in colonic fluid volume following supplementation [95]. In the study, fourteen healthy volunteers consumed kiwifruits twice daily versus an isocaloric control (maltodextrin) twice daily, for a total of 3 days. Relaxation time of ascending and descending colon, small bowel water content, colonic volume, gut transit time, and stool frequency and form were monitored via MRI scanning on the third day for a total of 7 hours. An increase in colonic fluid volume was observed as well as an increase in total colonic volume. Together, the data strongly suggests kiwifruit is an excellent option to induce laxation and relieve constipation, and should be considered as an effective alternative to other laxatives.

### Functional Gastrointestinal Disorders

Functional gastrointestinal disorders (FGID) are a classification of symptomatic gastrointestinal syndromes that are heavily related to gut-brain dysfunction without structural etiology [96]. These disorders mainly involve visceral hypersensitivity and are classified by location of symptomatic trigger [96]. FGIDs, including irritable bowel syndrome, are treated with a combination of dietary modification (i.e. a low fermentable oligo-, di-, mono-saccharides and polyols (FODMAP), and high fiber diet), psychological therapy, exercise, and medication regimen dependent on primary symptom predominance [97, 98]. Kiwifruit nutritionally meet these criteria for recommendations of a low FODMAP and high fiber diet.

Irritable bowel syndrome with constipation (IBS-C) is a type of IBS in which one experiences symptoms of abdominal discomfort or bloating with constipation [99]. There are several studies that investigate its use as a dietary supplement in patients with functional constipation or IBS-C, as compared to healthy controls. IBS-C patients consuming two kiwifruit daily exhibited decreased bowel transit time compared to placebo pill-matched as well as healthy controls [100]. This therapeutic effect is comparable or greater than the effect of psyllium husk in increasing the number of spontaneous bowel movements as well as decreasing need for laxative use [81-83]. Notably, kiwifruit consumption was also associated with improvement in IBS disease severity scoring and abdominal pain, suggesting potential as a therapeutic addition to current therapy [101].

Kiwifruit have also been proposed to decrease gastric symptoms of indigestion such as bloating [82]. The theoretical mechanism for this is related to actinidin content. Actinidin, a proteolytic enzyme, is proposed to aid with protein digestion and decrease symptoms of indigestion. A study comparing supplementation of two varieties of kiwifruit, one containing actinidin and one without, showed no change in gastrointestinal transit time following consumption of a steak

meal; however, the actinidin supplementation group had improvement in symptoms of digestive comfort, including bloating [102].

### Microbiome Implications

There is growing recognition that the microbiome plays an important role in the pathogenesis of disease. Consumption of certain types of diets and dietary components has been shown to profoundly influence disease mechanisms and can have a major influence on the communities of colonic microorganisms [103]. In fact, enhancement of colonic microbial composition is thought to mediate many of the beneficial health effects of kiwifruit. Kiwifruit have been shown to improve parameters of gut health via an increase in the commensal microbes *Coriobacteriaceae spp.*, *Bifidobacterium spp.*, and *Faecalibacterium prausnitzii* [54]. A four-week randomized double-blind placebo-controlled crossover trial demonstrated that the addition of kiwifruit-derived supplements, ACTAZIN™ L (low dose, green kiwifruit, 600 mg/day, manufacturer: Anagenix Ltd.), ACTAZIN™ H (high dose, green kiwifruit, 2400 mg/day, manufacturer: Anagenix Ltd.), and Livaux™ (gold kiwifruit, 2400 mg/day, manufacturer: Anagenix Ltd.), affected commensal microbe composition [54]. *Clostridiales* increased by 2-6% after Livaux™ supplementation in the healthy group. The abundance of the commensal microbe *Faecalibacterium prausnitzii* was significantly elevated (3.4-7%) in the functionally constipated group after Livaux™ supplementation. The clinical relevance of this finding is two-fold as *F. prausnitzii* is a butyrogenic microbe and low levels have been correlated with several gastrointestinal diseases [104]. These supplements were also tested clinically in another four-week crossover trial and were found to significantly increase bowel movements in healthy individuals [105]. Further, another in vitro study examined how whole kiwifruit affects the gut microbiota and found that gold and green kiwifruit increased the commensal microbe *Bifidobacterium spp.* and increased generation of SCFAs [53]. Another study investigating kiwifruit supplementation in patients with pre-diabetes demonstrated an increase in uncharacterized *Coriobacteriaceae spp.* which may play a role in polyphenol metabolism [106]. Together, this suggests that the main mechanism by which kiwifruit facilitates its digestive benefits are most probably through SCFA production via modification of the commensal microbiome, though other metabolic mechanisms may also play a role. Although it is difficult to isolate one dietary component as crucial in disease pathogenesis, these changes in microbiome composition are clinically relevant. Improvement in laxation coupled with increased butyrate concentrations could be beneficial for ulcerative colitis patients [54]. In individuals with prediabetes, the biomic changes improved vitamin C levels [106]. Dietary direction towards biomic balance can reduce markers of inflammation and may improve symptoms of FGIDs although further study is clearly warranted.

Fiber as a substrate for microbial communities is a key mechanism to increase numbers of beneficial bacteria and

reduce numbers of pathogenic bacteria [51, 52]. Soluble dietary fiber makes up the majority of colonic fermented fiber and increased intake is associated with an increase in SCFA production as well as an increase in the *Firmicutes: Bacteroidetes* ratio [107]. *Firmicutes* are mainly anaerobes and comprise a large portion of bacterial fermentation of luminally retained substrates including fiber [107, 108]. Kiwi fruit supplementation specifically increases abundance of *Firmicutes spp.* within the genera *Lactobacillus* and *Faecalibacterium* as well as another anaerobic fermenting genus, *Bifidobacterium* within the phylum *Actinobacteria* [54, 109]. Fermentation of dietary fiber by these anaerobes leads to SCFA production [110]. SCFAs promote hypoxia-inducible factor production by the local epithelium, which plays a key role in maintenance of the epithelial barrier [111, 112]. SCFAs also acidify the luminal environment and thus inhibit the conversion of primary bile acids to secondary bile acids [113]. Secondary bile acids are associated with up regulation of the production of cell proliferative markers and ROS, both mechanistically involved in carcinogenesis [114]. This mechanism of SCFA-mediated epithelial protection may be the mechanism by which dietary consumption of soluble fiber has a protective effect from the development of colorectal cancer [115]. While the potential benefits of soluble fiber in preventing localized colonic disease is evident, the presence of non-soluble fiber may contribute to the osmotic bulking that may assist with the treatment of symptomatic colonic disease.

### Conclusion

There is a growing body of evidence to support the beneficial effects of kiwifruit in a broad array of common ailments, including metabolic, cardiovascular, and gastrointestinal disease. Furthermore, there is evidence suggesting a beneficial role in healthy individuals. Further dietary intervention studies will be helpful to clarify the mechanisms of action of kiwifruit, and how these effects may improve specific symptoms and promote health. Although highly likely to be a beneficial effect on the intestinal microbiome, further investigation in this area is clearly needed. Overall, however, the supportive literature on kiwifruit strongly indicates a platform of potentially favorable health implications.

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