Livaux™ a novel, whole gold kiwifruit-based ingredient for promoting *Faecalibacterium prausnitzii* and microbiome balance

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Livaux™

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Executive Summary

Livaux™ is a wholefood-based nutritional ingredient option, crafted from the nutrient-dense New Zealand gold kiwifruit. It consists of a variety of bioactive components including fiber and polyphenolics, contributing to its prebiotic activity.

Livaux™ has recently been shown to increase the levels of *Faecalibacterium prausnitzii* (F. prau), a major beneficial, butyrate-producing bacterium, in functionally constipated humans. The relative distribution of the various genera and species of bacteria in healthy individuals is well described, and it has become apparent that an imbalance in the relative distribution of selected bacterial species is associated with selected diseases. Principal drivers of this microbiome imbalance include one or more of the following: a nutritionally defective diet associated with insufficient consumption of fermented foods, overuse of antibiotics, and use of anti-bacterial products. F. prau, a member of the Firmicutes phylum, accounts for approximately 5-15% of the total colonic microbiome. For over 10 years, a decreased intestinal number of F. prau has been linked to Crohn's disease (chronic, debilitating, inflammatory disease of the bowel), and more recently irritable bowel syndrome. Livaux™ is the only nutritional supplement (dietary or food) shown to increase the levels of F. prau in functionally constipated individuals, thus promoting the restoration of microbial balance. In addition, Livaux™ use is supported, in part, by the multitude of beneficial effects of whole gold kiwifruit for immune system support and antioxidant protection. Evaluation of Livaux™ in healthy individuals supports its use for increasing the frequency of bowel movements. Competitive analyses of Livaux™ compared to existing digestive health ingredients reveals a highly favorable profile that merits it consideration by product development professionals for inclusion in new or existing digestive and immune health products.

Introduction

Digestive and immune health are major product categories for functional food, nutraceutical, and dietary supplement product development professionals. In 2016, digestive health-positioned products (foods/drinks) reached approximately $55 billion (global retail sales), and accounted for the third largest product category in the $594 billion worldwide Health and Wellness market (global retail sales), only trailing products in the general well-being (eg multi-vitamins, etc) and weight-management categories [1]. In the US in 2016, digestive health-positioned products reached an estimated $2.5 billion in retail sales, ranking 4th behind sports/energy/weight loss ($12.6 billion), general well-being ($5.4 billion), immune/cold/influenza ($2.7 billion), and equivalent to heart-health product retail sales ($2.5 billion) [2].

Probiotics and fiber have dominated the scene and driven growth in the digestive health category while, simultaneously, suffering from significant class-specific limitations: existing probiotics are simply not sufficiently effective for most individuals seeking gastrointestinal relief, while the high fiber amount required for relief and other health benefits are simply too aggressive for many individuals to endure. In addition, the higher fiber doses are for acute symptomatic relief, and are generally not tolerated or sustained for long-term use. To address these challenges, a new functional food ingredient has been created from the New Zealand gold kiwifruit. This ingredient is Livaux™, and is the topic of this white paper.

Gold Kiwifruit

Overview

Although there are many species and cultivars of kiwifruit, by far, the most important commercial species accounting for virtually all international trade and consumption by consumers are green kiwifruit (*Actinidia deliciosa* cv. 'Hayward') and gold kiwifruit (*Actinidia chinensis* cv. 'Hort16A' and others) [3-5]. Aside from their color difference, green kiwifruit possess a bold, sweet and sour taste, while gold kiwifruit have a milder, sweeter taste.

The potential and substantiated health benefits of both major types of kiwifruit have been the subject of an increasing number of peer-reviewed studies since 1977 [5-9]. Among its many reported health benefits [5;7], green kiwifruit is most widely used as a gentle, safe, and effective nutritional intervention for gastrointestinal discomfort, especially constipation [10]. In contrast, consumption of gold kiwifruit has been linked to a) improved immunity in healthy older humans [9;11-13], b) increased antioxidant status in healthy humans [8;12;14;15], c) reduction in biomarkers of oxidative damage in healthy humans [14;16], d) improved iron status in healthy females with reduced iron stores [17], and e) mood improvement in young adult males with elevated total mood disturbance scores [15].

Kiwifruit Fiber Composition and Hydration Properties

The dietary fiber content of green (Hayward) and gold (Gold3, SunGold) kiwifruit is 3.0 g/100 g[1] and 1.4 g/100 g[2], respectively, and comprises approximately 1/3 soluble and 2/3 insoluble fibre [18].The soluble fiber consists of mostly pectic polysaccharides, and the insoluble is mostly cellulose and hemicelluloses along with a small amount of pectin. The pectin molecules, in their role as structural components of the kiwifruit cell wall, bestow the superior hydration benefits of kiwifruit fiber.

Interestingly, kiwifruit fiber has unique hydration properties. It has the capacity to swell or 'gel' (ie, the volume fiber has in water after passively settling), reaching over three times its volume in the original fruit [19]. Compared to rehydrated dietary fiber preparations, the swelling capacity of freeze-dried kiwifruit fiber is twelve times higher than wheat bran, more than six times higher than apple fiber, and one and a half times higher than psyllium [19].

Kiwifruit fiber also has high water retention capacity- the amount of water that is bound to insoluble fiber and is not separated from fiber by centrifugation [20]. The water retention capacity of kiwifruit fiber is 12-13 g water/g insoluble fiber, which is about twice that of apple fiber and four times that of wheat bran. The hydration properties of the fiber affect the dynamics of macronutrient absorption, reducing mixing in the bowel and diffusion [21;22]. Kiwifruit fiber may also add to fecal bulking [19]; however, it is also completely fermentable by the gut microflora and therefore may play a significant role in the modulation of the composition of the microflora [19].

1. United States Department of Agriculture, Food Composition Database: https://ndb.nal.usda.gov/ndb/search/list (accessed June 20, 2017)
2. United States Department of Agriculture, Food Composition Database: https://ndb.nal.usda.gov/ndb/search/list (accessed June 20, 2017)

By comparison, the hydration properties of inulin and fructose oligosaccharides (FOS) are less robust due to their chemical structures and properties. Inulin is a naturally occurring, non-structural carbohydrate (fructose) polymer characteristic of most plants. It is believed to be used as an energy storage molecule. Due to its typical chain length (ie degree of polymerization) of ~ 60 fructose units, it is very soluble in aqueous solution, and thus is not a very effective hydrator. FOS is even more water soluble than inulin, and thus is resistant to hydration. Thus, the greater molecular size (degree of polymerization), different subunit composition, and function as a structural component of pectin and related molecules largely accounts for the excellent hydration properties of kiwifruit fiber.

Gold Kiwifruit as a Prebiotic Substrate

The emerging role of gold kiwifruit as a prebiotic substrate was first described by Parkar et al (2012), who reported that fecal fermentations *in vitro* of gold kiwifruit increased the growth of Bifidobacterium spp. by 0.9 $\log_{10}$ colony forming units/ml [23;24]. More recent research on a novel gold kiwifruit cultivar ('Zesy002', Gold3) indicated a substantial increase in Bacteroides spp., Parabacteroides spp., and Bifidobacterium spp. levels, along with a concomitant increase in propionate production *in vitro* (simulated colonic fermentation) [25]. *In vivo* administration of homogenized gold kiwifruit to healthy rats improved a variety of markers of intestinal barrier function (eg mucin-2 and 3, others) [26]. Recent work by Ansell et al has shown, for the first time, that administration of gold kiwifruit to healthy adults for 4 weeks increases their frequency of bowel movements by approximately 1 per week [27], along with increasing the level of *Faecalibacterium prausnitzii* (F. prau), a major beneficial bacterial species in the human intestine, in functionally constipated adults [28].

What is *Faecalibacterium prausnitzii?*

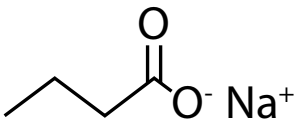
Of the thousand or so bacterial species that reside in the human gut (primarily the large intestine), only a few are very special. F. prau is one of those very special bacterial species [29;30]. F. prau, a member of the Firmicutes phylum, accounts for approximately 5–15% of the total colonic microbiome [31]. For over 10 years, a decreased intestinal number of F. prau has been linked to Crohn's disease (chronic, debilitating, inflammatory disease of the bowel) [30;32–34], and more recently irritable bowel syndrome [35].

Although being a major microbial inhabitant of the human gut is important, F. prau brings so much more to the digestive health and wellness table. First, F. prau readily ferments soluble fiber and polyphenolic compounds, as evidenced by reported increases in bacterial indices following dietary intervention in humans [36–38]. Second, F. prau is linked to increased production of butyrate, a short-chain fatty acid that has multiple beneficial effects within the intestine including anti-inflammatory and immune-enhancing activities, along with a plethora of extra-intestinal effects [37;39–41]**(Table 1)**. Only a limited number of intestinal bacteria are able to produce butyrate in meaningful quantities. Third, reduced levels of F. prau have been associated with chronic constipation, celiac disease (auto-immune reaction to gluten), irritable bowel syndrome, and inflammatory bowel disease including Crohn's disease and ulcerative colitis [32–35;42]. This suggests that F. prau modulation / replenishment might be beneficial for these digestive conditions. This idea is supported by studies in murine models that reported short-term administration of F. prau protected against chemically-induced inflammation in mice [43] and reduced adipose-tissue inflammation in high-fat fed mice [44].

Under most conditions, F. prau is an obligate anaerobe (unable to survive in the presence of oxygen), a major obstacle for widespread commercialization as a probiotic. Previous efforts to boost F. prau levels in humans with a common prebiotic (fructo-oligosaccharides) have been unsuccessful [45]. Since many individuals with inflammatory bowel disease (and other digestive tract dysfunction) cannot tolerate efficacious amounts of inulin or other fermentable fibers, it is safe to say that, until now, taking a prebiotic to increase the level of F. prau has been futile.

How does F. prau exert its many unique beneficial effects? Most likely, this involves several complementary actions including the production of butyrate and other anti-inflammatory molecules (eg interleukin-10) and subsequent anti-inflammatory activity [32]. In addition, F. prau is able to stimulate the recruitment / activation of regulatory T cells [30;32;46;47]. Other work has found that F. prau is able to metabolize pectin and uronic acids as substrates for growth, and both are well known constituents of gold kiwifruit [19;48].

Table 1. Summary of the Intestinal and Extra-Intestinal Effects of Butyrate[3]

Butyrate (Sodium salt) **CH_3-CH_2-CH_2-COO^- Na^+**	Is mainly taken up by the colon epithelial cells, only small amounts reach the portal vein and the systemic circulation
	**Intestinal Effects** • Is the preferred energy source for the colon epithelial cells • Decreases the pH of the colon, which decreases bile salt solubility, increases mineral absorption, decreases ammonia absorption, and inhibits growth of pathogens • Stimulates proliferation of normal colon epithelial cells • Prevents proliferation and induces apoptosis of colorectal cancer cells • Affects gene expression of colon epithelial cells • Plays a protective role against colon cancer and colitis • Improves the gut barrier function by stimulation of the formation of mucin, anti-microbial peptides, and tight-junction proteins • Interacts with the immune system • Has anti-inflammatory effects • Stimulates the absorption of water and sodium • Reduces oxidative stress in the colon **Extra-Intestinal Effects** • Enhances cardiovascular and metabolic function • Enhances cognitive function • Has anti-inflammatory effects • Reduces oxidative stress • Enhances energy expenditure • Linked to many benefits of ketogenic diet • Enhances mitochondrial biogenesis

3. Table compiled and adapted from [37;39–41].

Livaux™

Overview and Uniqueness

Livaux™ is a food-quality ingredient derived entirely from New Zealand gold kiwifruit *(Actinidia chinensis),* with pre-clinical and clinical data supporting its use as a digestive health ingredient. The process to create Livaux™ begins with premium gold kiwifruit sourced exclusively from Zespri®-approved growers and harvested from the pristine orchards of New Zealand – removing the skin and seeds - then cold-drying the bright-gold nutritious flesh into unadulterated, free-flowing powder, for use in functional foods, nutraceuticals, and dietary supplements. The process to create Livaux™ is gentle and chemical / solvent-free. This results in a final product that is, essentially, lyophilized gold kiwifruit powder, chemically unchanged from the pure, non-GMO, additive-free *Actinidia chinensis,* from which it is derived. Livaux™ is Kosher-certified, and is also available as an organic ingredient.

Livaux™ contains a unique combination of bioactive nutrients, that effectively and gently support the digestive and laxation processes. These constituents include

1) Soluble and insoluble fiber (approximately 10%; recognized universally as health-promoting ingredients),

2) Polyphenolic compounds, that can act either as direct antioxidants, or indirect antioxidants (via upregulation of the transcription factor Nrf2 [47]),

3) Prebiotic substrates including fiber, carbohydrates, and polyphenolics (as microbiome modulators: ie promoting growth of beneficial bacteria and /or inhibiting the growth of pathogenic bacteria).

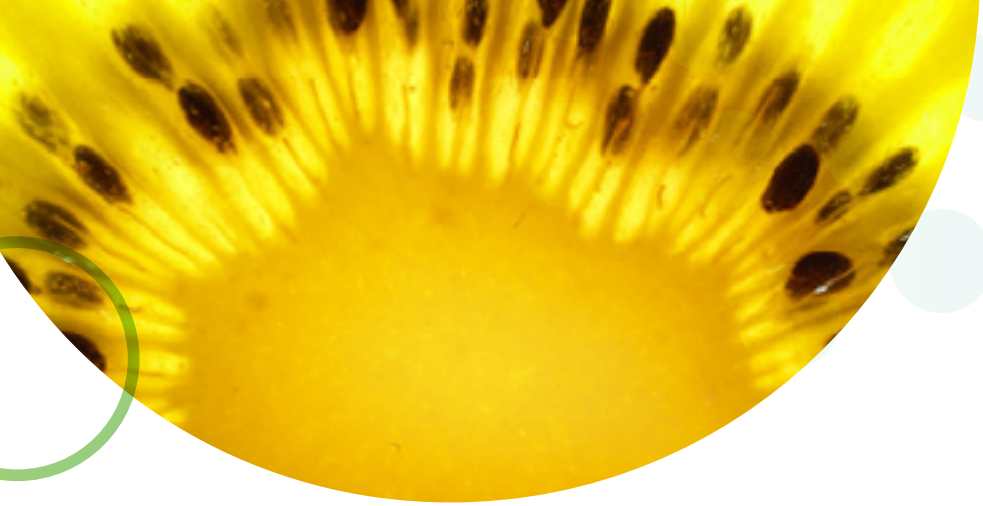
A growing amount of pre-clinical and clinical research has been conducted on the beneficial effects of gold kiwifruit on human health (see above), including a large body of research on individual constituents and classes of compounds. This research supports the idea that the individual kiwifruit constituents contribute individually and in combination to the overall health effects, offering a variety of digestive, microbiome-modulating, and immune-enhancing (and other) health benefits.

Clinical Evidence to Support Livaux™: Increase in F. prau *Relative Abundance*

A randomized, double-blind, placebo-controlled, crossover study was conducted utilizing a single dose of Livaux™ administered to healthy and functionally constipated individuals [27]. In this clinical study, participants provided fecal samples at the beginning and end of each intervention period for microbiome compositional analyses [28]. The relative abundance of the prevalent bacterial groups was determined following DNA isolation and ribosomal RNA gene sequencing, and the data on healthy and functionally constipated cohorts were analyzed separately. The effects of each treatment (ie Livaux™ and placebo) on microbial composition was determined by comparing the average abundance of each bacterial genus (>1% abundance in at least one of the 8 samples) following treatment with the average value before treatment.

There were marked differences between the microbial composition of the healthy and functionally constipated subjects. Thirty-two genera were detected at >1% abundance in at least one sample, 10 of which differed significantly between the healthy and functionally constipated cohorts [28]. In agreement with other studies, the ratio of Firmicutes to Bacteriodetes differed between the two groups: ratio in healthy subjects = 2.3 and ratio in functionally constipated subjects = 3.2.

The most striking result was observed in the functionally constipated group, in which the relative abundance of F. prau increased by approximately two-fold in response to Livaux™ administration (3.4% to 7.0%; P = 0.024). The individual participant data is provided in **Figure 2,** which shows that 8 of the 9 subjects exhibited an overall increase in the % relative abundance of F. prau.



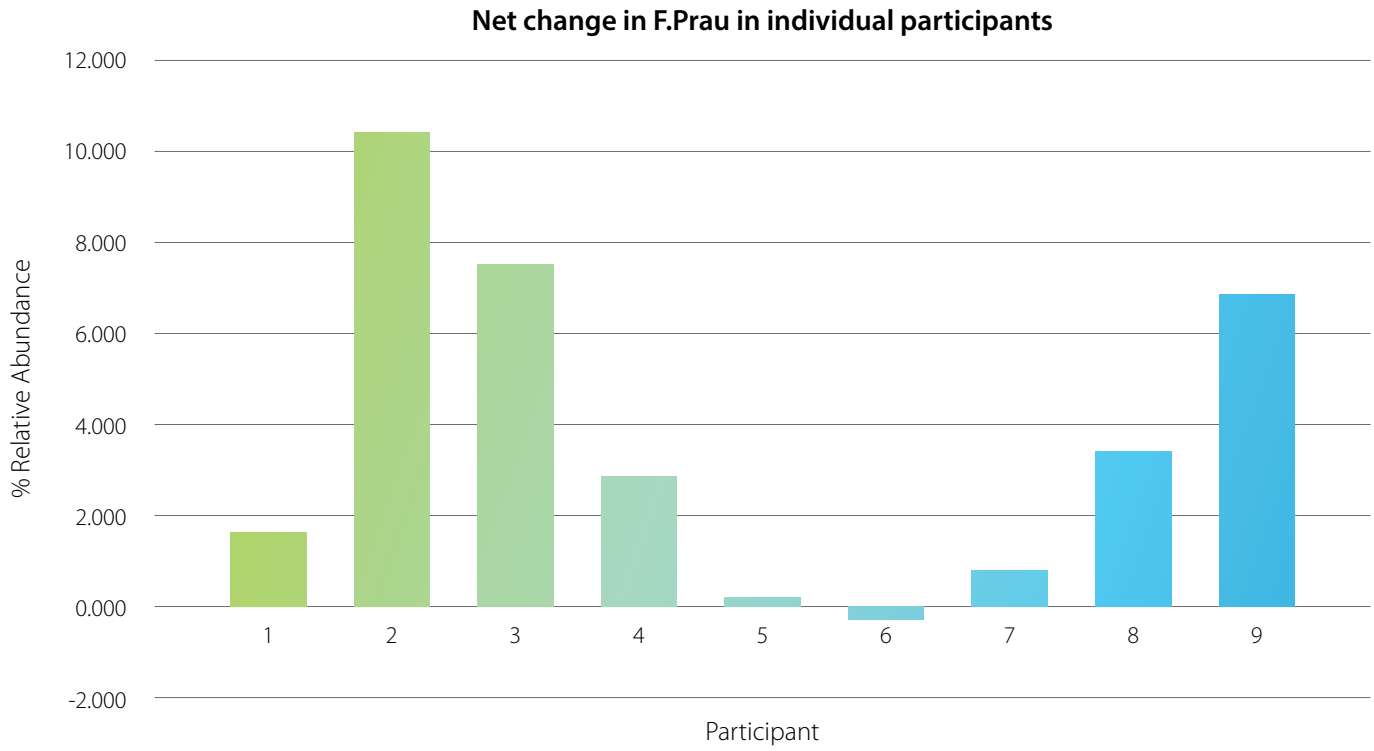


Figure 2. Individual changes in the relative abundance of *F. prausnitzii* in the functionally constipated subjects. The mean relative abundance of F. prau increased by approximately two-fold (3.4% to 7.0%; P = 0.024) in response to Livaux™ administration for 4 weeks. The individual participant data is provided in **Figure 2** (above), which shows that 8 of the 9 subjects exhibited an overall increase in the % relative abundance of F. prau. Figure from [50].

Clinical Evidence to Support Livaux™: Frequency of Bowel Movements

The clinical study discussed above also demonstrated that in healthy individuals (n=19), at a dose of 2,400 mg daily, Livaux™ administration (4 weeks) produced a statistically significant increase in the number of daily (weekly) bowel movements when compared to washout as baseline (P = 0.009; 10.5% increase over washout). This is the first clinical study to report a beneficial effect of gold kiwifruit on laxation in any human population. There was no significant change in the Bristol Stool Chart scores suggesting that while the number of stools increased, their form was not adversely affected (ie did not induce looser stool form). No significant change in the frequency of bowel movements were observed in the functionally constipated cohort (n=9), presumably due to insufficient statistical power. A summary of the study design, outcome measures along with selected results are presented in **Tables 2 and 3.**

Table 2. Summary of the Study Design Features and Outcomes of the Livaux™ Clinical Trial

SUBJECTS	STUDY DESIGN	DOSE	PLACEBO	OUTCOME MEASURES	OBSERVED BENEFITS
19-Healthy (38 yr mean; 23 mean BMI; 2/19 Male) 9-C3 Functionally constipated (44 yr, mean; 25 mean BMI;1/9 Male)	Randomized, double-blind, placebo-controlled crossover 2-week washout, 4 week each intervention	2,400 mg Livaux™ daily	Isomalt (4 x 600 mg caps)	*Primary:* significant increase in stool frequency; *Secondary,* Clinical: 1) improvement in stool form 2) changes in faecal microbial populations.	2,400 mg dose of Livaux™ significantly increased stool frequency compared to baseline in healthy individuals. Livaux™ significantly increased *F. prausnitzii* (F. prau) levels by approximately 2-fold in the functionally constipated group. Eight of the nine subjects in functional constipated cohort had net increases in F. prau.

Post-hoc analysis was carried out on a sub-group of defined responders (n=14/19 subjects in healthy cohort; 74% responded), defined as those individuals showing an increase of at least 1 bowel movement per week over the preceding washout period on at least one of the non-placebo interventions. The statistical analysis of this sub-group indicated a statistically significant increase in the number of bowel movements in response to 2,400 mg Livaux™ (P = 0.001, 16.5% increase over washout). A summary of results is presented in **Table 3.**

Table 3. Livaux™ Clinical Trial: Number of Bowel Movements and Percent Change from Washout in the Healthy Cohort and Responder Sub-Group

HEALTHY GROUP (N = 19)	DAILY BOWEL MOVEMENTS	WEEKLY BOWEL MOVEMENTS	INCREASE PER WEEK OVER WASHOUT	% INCREASE OVER WASHOUT	P, ANOVA	P VS WASHOUT
Washout, Overall Mean	1.08	7.6	0	0	0.002	–
Placebo	1.12	7.8	0.2	2.6	–	0.377
Livaux™ 2,400 mg	**1.20**	**8.4**	**0.8**	**10.5**	–	**0.009**
RESPONDER SUB-GROUP[4]	**DAILY BOWEL MOVEMENTS**	**WEEKLY BOWEL MOVEMENTS**	**INCREASE PER WEEK OVER WASHOUT**	**% INCREASE OVER WASH OUT**	**P, ANOVA**	**P VS WASHOUT**
Washout, Overall Mean	1.18	8.3	0	0	< 0.001	–
Placebo	1.27	8.9	0.6	7.2	–	0.117
Livaux™ 2,400 mg	**1.38**	**9.7**	**1.4**	**16.9**	–	**< 0.001**

4. Participants were classified as responder or non-responder. Responders were defined as subjects who exhibited an increase of ≥ 1 bowel movement per week over the preceding washout period on at least one of the non-placebo interventions. Data from Ansell et al (2015) [27]. Livaux™ was designated by Ansell et al as Gold kiwifruit powder in their publication [27].

It is important to note that an increase of ≥ 1 bowel movement per week in a symptomatic population is considered a clinically meaningful magnitude of effect by the United States Food and Drug Administration [51], and would significantly improve the symptoms of sufferers of mild or occasional constipation. Livaux™ (2,400 mg/day) produced this magnitude of effect in the healthy cohort. Due to poor recruitment of individuals into the functionally constipated cohort (primarily due to potential subjects refusing to abstain from eating kiwifruit, an absolute exclusion criterion), there was insufficient statistical power to perform an appropriate analysis.

No published data are available that identifies a minimally efficacious daily quantity for whole green (or gold) kiwifruit for increasing bowel movement frequency. However, 2,400 mg of Livaux™ is approximately the equivalent of 25–30% of a whole gold kiwifruit (by weight). Twenty-four hundred mg of Livaux™ produced a clinically meaningful increase in bowel movements in healthy adults. Thus, a daily dose of 2,400 mg of Livaux™ is ***functionally equivalent,*** in terms of laxation benefit, to 2 whole green kiwifruit, keeping in mind that 1 whole fresh kiwifruit (green and gold) contains a substantial amount of water.

Safety of Kiwifruit and Livaux™

The Natural Standard Monograph (2011; now called Natural Medicines) reports kiwifruit to be likely safe when consumed in amounts naturally found in foods. A number of clinical studies have been conducted on both whole green and gold kiwifruit, and all have reported both varieties of kiwifruit (2 kiwifruit per day) to be safe and well tolerated (reviewed in [6–9]). Consumption of Livaux™ at 2,400 mg for 28 days was well tolerated with no serious adverse events reported [27]. Twenty-four hundred mg of Livaux™ is approximately the equivalent of 25% a whole kiwifruit, so this amount falls well within the clinically evaluated daily intake level mentioned above, and is considered as safe.

Kiwifruit is suitable for all age groups. However, for a very small number of individuals, kiwifruit may trigger an allergic response. Virtually all food groups can cause an allergic reaction in some sensitized individuals. Globally, the incidence of food allergy is reported to be increasing [52;53]. However, the prevalence of kiwifruit allergy in the general population has been estimated to be less than 2% [54]. People with allergies to latex, birch pollen, and dust mites are more likely to be allergic to kiwifruit. Care should be taken when first introducing kiwifruit or new varieties of kiwifruit to children, particularly those with other known food allergies. People with a known kiwifruit allergy should avoid all kiwifruit.

Who Would Benefit from Livaux™?

The following individuals are likely to benefit from regular supplementation with Livaux™:

- those individuals with a reduced level of F. prau
- those individuals prone to mild-moderate constipation, including the elderly and those on certain prescription medications
- healthy men and women who desire to maintain the regularity and quality of their bowel daily movement(s) and maintain a healthy intestinal microbiome
- those individuals with reduced immune function, or who desire immune support for their upper respiratory tract
- those individuals who wish to increase their antioxidant intake, including Vitamin C and polyphenolics
- those individuals who suffer from mild-moderate stress
- Children who desire a natural source of Vitamin C, immune support, or who are constipated.

Recommended Use / Advantages of Livaux™
To increase the number of F. prau
To support healthy gut microbiome modulation by providing prebiotic material to indigenous bacteria and in combination with commercial probiotic(s)
To promote and gently facilitate bowel regularity
To gently increase the number of daily/weekly bowel movements
To offer an ingredient that simulates whole gold kiwifruit
To provide a natural source of fiber, Vitamin C, and polyphenolic compounds
To offer a natural, clean-label ingredient
To offer an ingredient that is effective with no major side effects
To offer an ingredient that is safe for children
To offer an ingredient that possesses excellent organoleptic properties (ie appearance, taste, aroma, texture/feeling in the mouth)

Formats and Applications
Livaux™ is a compatible ingredient for inclusion with the following:
Digestive health formulations
Detoxification formulations
Formulation with probiotics
Green food blends (capsules, tablets, powders etc.)
Fruit and veggie formulations
Whole food vitamin and mineral complexes
Enzyme formulations
Super-fruit products
Fiber formulations

Dosage Recommendation
Restorative Microbiome Effect
To restore levels of *Faecalibacterium prausnitzii,* Livaux can be taken up to **2,400 mg per day**
Digestive Discomfort
To facilitate laxation and increase stool frequency, Livaux™ can be taken up to 2,400 mg per day until discomfort passes.
Digestive Health Maintenance
For ongoing digestive health maintenance, Livaux™ can be taken at 600 mg per day to provide nutrients on a consistent basis to help regularity, and support a healthy gut environment.
Digestive Health Companion Formulation
Livaux™ in combination with one or more probiotic(s) to promote the selective growth of beneficial bacteria
A minimum of 50 mg Livaux™ per billion colony-forming units of probiotic[5]; or
A minimum of 500 mg Livaux™ in formulation with >10 billion colony forming units of probiotic[6]

Nutrient Composition (Energy, vitamins, minerals)

The selected nutrient composition of both major commercial varieties of whole kiwifruit has been widely reported [6;55]. Nutrient composition databases compiled by the US Department of Agriculture[7] and The New Zealand Institute for Plant & Food Research and Ministry of Health[8] are also freely available. Representative values for selected macro- and micronutrients is provided in **Table 4.** This table also provides comparative values for other commonly consumed fruits (apples, bananas, strawberries, and blueberries). It is important to keep in mind that the values shown are averages and approximate, as differences in many environmental factors could affect the values listed. The nutrient composition of Livaux™ is provide in **Table 5.**

5. Anagenix internal data
6. Anagenix internal data
7. https://ndb.nal.usda.gov/ndb/search/list (accessed 5/7/2017)
8. http://www.foodcomposition.co.nz/concise-tables (accessed 5/7/2017)

Table 4. Selected Nutrient Composition of Green and Gold Kiwifruit[a] Along with Other Commonly Consumed Fruit[9]

NUTRIENT	GREEN KIWIFRUIT *(Actinidia deliciosa)*	GOLD KIWIFRUIT *(Actinidia chinensis)*	ORANGE (NAVEL) *(Citrus sinensis)*	APPLE WITH PEEL *(Malus domestica)*	BANANA *(Musa acuminata)*	STRAWBERRIES *(Fragaria × ananassa)*	BLUEBERRIES *(Vaccinium spp.)*
Energy (kJ)	255	251	207	218	371	136	240
Carbohydrate (g)	14.66	14.23	12.54	13.81	22.84	7.68	14.49
Fibre, total dietary (g)[†]	3.39	2.0	2.40	2.70	2.40	2.30	2.70
Insoluble DF (g)	2.60	1.4	1.00	2.00	1.80	1.70	2.40
Soluble DF (g)	0.80	0.5	1.40	0.70	0.60	0.60	0.30
Sugars, total (g)	8.99	10.98	8.50	10.39	12.23	4.89	9.06
Vitamin C (ascorbic acid) (mg)	92.7	105.4	59.1	4.6	8.7	58.8	9.7
Vitamin E (α-tocopherol) (mg)	1.46	1.49	0.15	0.18	0.10	0.29	0.57
Vitamin K (phylloquinone) (µg)	40.3	5.5	0	2.2	0.5	2.2	19.3
Folate (µg DFE)	25	34	34	3	20	24	6
Beta carotene (mg)	52	43	87	27	26	7	32
Lutein+zeaxanthin (mg)	122	114	129	29	22	26	80
Potassium (mg)	312	316	166	107	358	153	77
Copper (mg)	0.13	0.15	0.04	0.03	0.08	0.05	0.06

[†] *Nutrient values for kiwifruit are raw, per 100 g of edible portion DF, dietary fiber; DFE, dietary folate equivalents Table from [6].*

9. Nutrient values for the edible portion of fruit from [6] and United States Department of Agriculture, 2011.

Table 5. Representative Macronutrient Content of Livaux™

TYPICAL NUTRITION INFORMATION – *SUBJECT TO NATURAL AND SEASONAL VARIATIONS*		
SERVING SIZE: 2400 MG (1 SERVINGS DAILY)[10]		
	Average Quantity per Serving	**Average Quantity per 100 g[11]**
Energy, kJ	34	1420
Protein, g	0.094	3.9
Fat, total, g	0.043	1.8
Saturated, g	0.008	0.34
Unsaturated, g	0.034	1.4
Monounsaturated, g	<0.10	<0.10
Polyunsaturated, g	0.034	1.4
Carbohydrate, g	1.7	71
Sugars, total, g	1.4	58
Glucose, g	0.65	27
Fructose, g	0.74	31
Lactose, g	<0.05	<0.05
Maltose, g	<0.05	<0.05
Sucrose, g	<0.05	<0.05
Dietary fiber, g	0.24	9.8
Insoluble fiber, g	0.21	8.8
Soluble fiber, g	0.024	1.0
Sodium, mg	0.43	18
Total phenolics, mg gallic acid equivalents (GAE)	26.4	1100

10. A dose of 2,400 mg of Livaux™ has been shown in a clinical trial to facilitate increased bowel movements in healthy individuals [27].
11. Based on calculation from average quantity per 100 g.

WHY LIVAUX™?

Advantages vs Competitive Ingredients

Compared to other options, Livaux™ is the superior, overall choice based on the most important criteria to evaluate / compare individual ingredients for digestive and immune health. Currently, there are limited clinical data with other food ingredients (ie prebiotic fiber or to restore levels of *Faecalibacterium prausnitzii*, Livaux can be taken up to 2,400 mg per day.) to significantly elevate the levels of F. prau in any population. High-dose inulin (10g/day) for 16 days produced a reported net increase of about 4% (relative abundance) in F. prau [56]. In addition, Finegold et al 2014 reported that xylo-oligosaccharides (XOS) increased F. prau, but only from baseline through to 4 weeks, after which the level dropped and plateaued for the remainder of study [57].

As an ingredient derived from whole gold kiwifruit, Livaux™ is novel compared to the existing, more mature gut and digestive health category options, with a greater diversity of collective, relevant claims along with a clear message of differentiation (eg ability to increase F. prau levels in functionally constipated individuals; ability to increase laxation in healthy individuals).

When considered, in total, with the clinical results obtained with whole gold kiwifruit, the clinical substantiation of Livaux™ supports its use in
a) healthy,
b) elderly,
c) functionally constipated individuals.

The versatility and organoleptic properties of Livaux™ are superior, resulting in compatibility with multiple delivery formats. This is critical for acceptance by product development professionals and consumers. A major strength of Livaux™ is its potential for clean-label and sustainability benefits. Finally, two of the most important criteria, effective dose (2,400 mg/day) and cost per dose clearly support consideration of Livaux™ over competitive ingredients.

Effective doses for fibers are known to be very high (~38 g/day men; ~25 g/day women), while effective doses for probiotics for the clinical improvement of digestive health symptoms are not clearly defined. The recommended doses vary for individual probiotic strains and depends on whether their use is for digestive health maintenance or relief of symptoms.

Table 6. Competitive Analyses of Livaux™ vs Other Ingredients in Market Space

CRITERIA	LIVAUX™	WHOLE FRUIT	PREBIOTICS	PROBIOTICS	FIBER	ENZYMES
Novelty	5	1	2	4	2	2
Ability to differentiate from competitors	5	4	2	3	2	2
Diversity of marketing claims	4	2	3	2	3	2
Scientific substantiation of claims	2	4	3	2	5	2
Compatibility with multiple delivery formats	5	1	3	4	3	3
Convenience of use by consumers	4	3	3	4	1	3
Clean label potential	5	5	3	4	3	2
Sustainability potential	5	5	4	5	4	3
Effective dose (higher score = lower dose)	3	2	1	1	1	2
Cost per effective dose (higher score = lower cost)	3	4	4	2	4	2
Total Score	**41**	**28**	**28**	**31**	**28**	**23**

All criteria scored on a scale from 1 (minimum, least) through 5 (maximum, most). Safety, regulatory, and competitive landscape are not listed as criteria for scoring, since these criteria are viewed as equivalent for all ingredients.

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