Kids Digestive Health & Immunity Support

with Livaux® Inside

Livaux®

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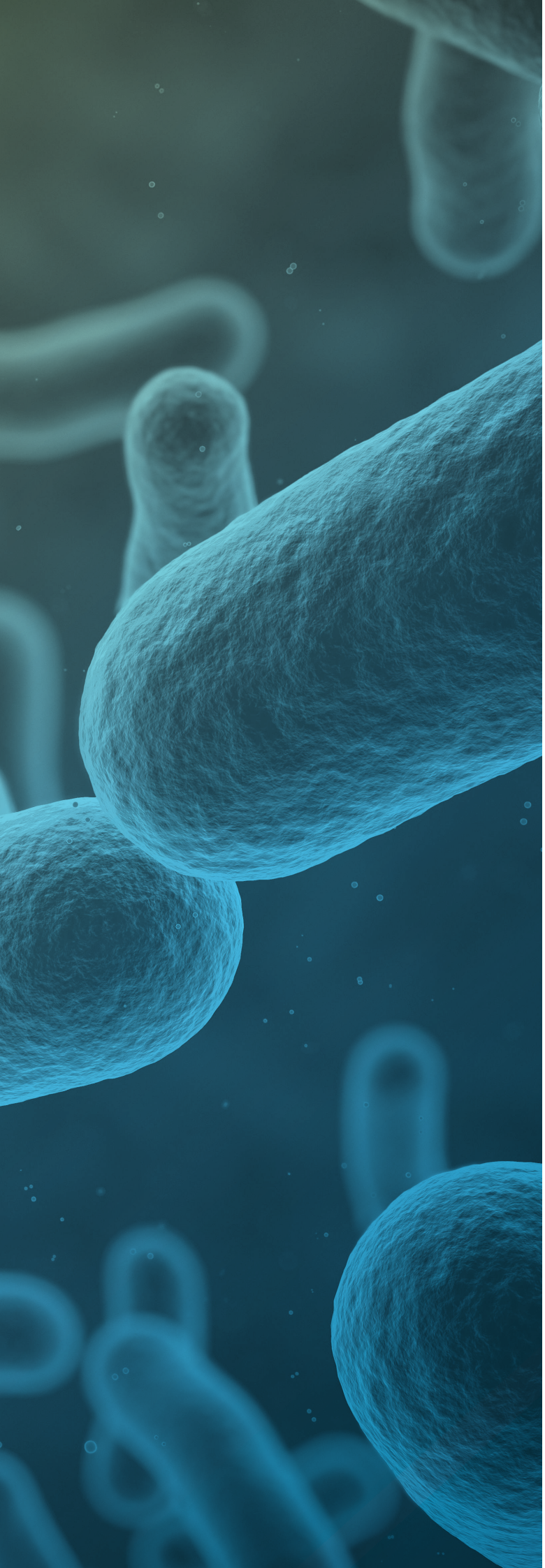
Livaux® for kids – digestive and immune health support

A lot of kids suffer from digestive discomfort and/or need a boost for their immune system. Livaux® provides key bioactives from gold kiwifruit to support digestive health (through improving bowel regularity and feeding the good bacteria) which in turn supports the immune system. The inclusion of a well-studied, shelf-stable probiotic, *Bacillus coagulans* BC-30, provides an additional boost to the digestive and immune systems.



The Anagenix Concept

Children often experience digestive discomfort and the prevalence of constipation in children can be as high as 36% (Afzal, Tighe, & Thomson, 2011) (Xinias & Mavroudi, 2015). They are also quite susceptible to colds and flus, with children reported to have 4 – 6 colds/flus per year (Skinner, 2012).

Livaux® is a great tasting, kid-friendly ingredient derived from the nutrient-rich gold kiwifruit. Livaux® provides key bioactives from gold kiwifruit to support the immune system (reducing the symptoms and duration of colds and flus) and the digestive system (improving bowel regularity and feeding good bacteria). The inclusion of a well-studied, shelf-stable probiotic, *Bacillus coagulans* GBI30, 6086 (Ganeden BC[30]), provides an additional boost to the digestive and immune systems.

Active Ingredients Science Summary

Livaux®

Livaux® is a high-quality powdered ingredient derived entirely from New Zealand gold (Gold3) kiwifruit. The proprietary processing technology gently converts the nutrient-dense gold kiwifruit into a free-flowing powder which is packed full of the key bioactives from the whole fruit.

Gold kiwifruit is able to enhance the immune response and help ameliorate the symptoms of colds and flus. These effects are via the direct actions of kiwifruit polyphenols and vitamins; as well as indirect actions of kiwifruit carbohydrates and polyphenols fermented by colonic microbiota, which promotes the growth of beneficial microbes and the production of short chain fatty acids (SCFAs).

Livaux® contains these essential gold kiwifruit carbohydrates, vitamins and polyphenols which are thought to be responsible for the immune responses observed in the *in vitro, in vivo* and human studies described below.

Livaux® also supports a healthy digestive system by promoting bowel regularity and increasing the levels of good bacteria in the gut. A healthy digestive system in turn supports a healthy immune system.

Whole gold kiwifruit research

In 2011, Skinner et al., reported that a gold kiwifruit puree enhances both T helper type 1 and 2 immune responses via enhanced production of IgG antibody and the cytokine, IL-5, in mice. A gold kiwifruit juice concentrate, which contained less dietary fibre and polyphenols, had no effect on the immune response in the same mouse model.

Following this research, Hunter, et al., 2012 and Skinner, 2012 reported the results of two clinical trials which examined the effects of gold kiwifruit consumption on cold and flu symptoms:

- In pre-school children (2 – 5 years), gold kiwifruit consumption (2 servings per day) resulted in an overall reduction in the incidence of cold and influenza-like illnesses as well as a reduction in their symptoms.
- In older adults (≥ 65 years), gold kiwifruit consumption (2 fresh plus 2 freeze-dried per day) significantly reduced head congestion, sore throat symptoms and plasma lipid peroxidation, and significantly increased plasma vitamin C, α-tocopherol and lutein/zeaxanthin concentrations, and red cell folate concentrations.

A summary of *in vitro, in vivo* and human studies on kiwifruit with respect to immunity was published in 2013 in Advances for Food and Nutrition Research (Skinner, Bentley-Hewitt, Rosendale, Naoko, & Pernthaner, 2013). In addition to the work mentioned above, the publication discussed the following:

- *In vitro* studies
  - Direct antimicrobial effect of extracts from gold kiwifruit has been shown.
  - Green kiwifruit was shown to increase the production of gastrointestinal defensins (human beta defensin-1 and -2).
    - This increase is thought to be mediated through SCFA production.
    - Gold kiwifruit was not evaluated in this study for its effect on defensins, however gold kiwifruit is known to stimulate the production of SCFAs.
  - Green and gold kiwifruit significantly reduced the intensity of barrier damage *in vitro*.
  - Aqueous extracts of green and gold kiwifruit reduced the levels of proinflammatory cytokines (TNF-α and IL-1β) in LPS-stimulated human monocytes and whole blood.
- *In vivo* studies
  - Rats fed 100 g of kiwifruit had a higher percentage of primed γδ T cells compared to control rats.
  - Kiwifruit extracts significantly enhanced intestinal mucosal and serum antibody responses to vaccines and promoted IFN-γ and natural killer cell activity.
- Human studies
  - Healthy, but fatigued-feeling adults were given either 3 gold kiwifruit, 3 bananas, a vitamin C supplement or no treatment daily for four weeks.
    - Gold kiwifruit consumption led to an increase in the % of CD8+ T cells and an increase in the numbers of naïve T cells and CD8+ CD28+ T cells.
    - There was also a significant reduction in the age of T cells in the gold kiwifruit group compared to baseline, whereas there was an increase with the banana group. No significant effect was seen with vitamin C or no treatment.
    - Subjects reported feeling significantly less fatigue, less skin dryness, better skin condition and less eye fatigue following kiwifruit consumption.

Livaux® specific research

Microbiome Balance – Clinical Study

Acting as a precision prebiotic, Livaux® has been shown in a clinical study to increase the abundance of the beneficial gut bacteria, *Faecalibacterium prausnitzii (F. prau),* to restore balance to the gut microbiome (Blatchford, et al., 2017).

Functionally constipated individuals were given 2,400 mg of Livaux® daily for four weeks. At the end of the 4-week treatment period, *F. prau* abundance in the participants' stool samples significantly increased (P = 0.024) from 3.4% - 7.0%, a two-fold increase (Figure 1). Further, 8 of the 9 participants showed a net increase.

F. prau is a beneficial bacterium with significant importance for gut flora balance. *F. prau* is one of the most abundant bacteria in the human gut ecosystem. It has anti-inflammatory properties and is a major butyrate producer. Butyrate is a short chain fatty acid which has numerous health benefits, including being the major energy source for colonocytes and having anti-inflammatory activity. Low numbers of *F. prau* have been associated with irritable bowel syndrome (IBS), inflammatory bowel diseases (IBD), coeliac disease, chronic constipation, GI cancer, diabetes and even allergies. Healthy levels of *F. prau* is therefore desirable for supporting healthy immune and digestive systems.

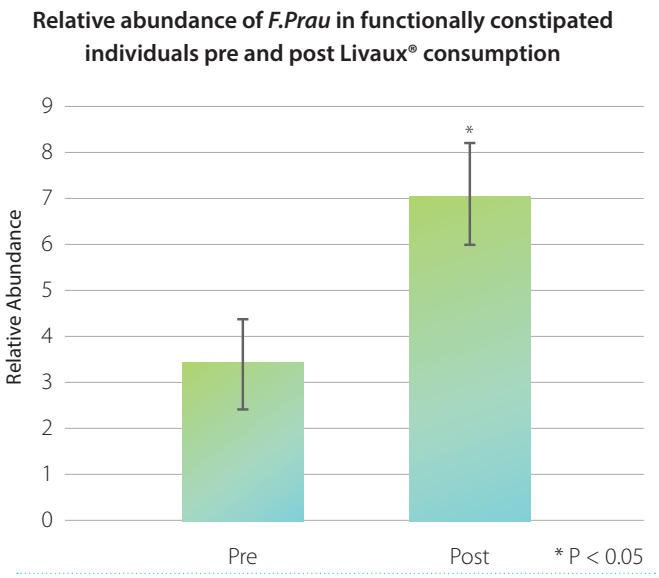


Figure 1: Change in F. prau abundance following Livaux® consumption

Bowel Regularity - Clinical Study

Livaux® has also been shown in a clinical study to increase stool frequency, without affecting stool form, to help maintain healthy bowel regularity (Ansell, et al., 2015).

Healthy participants were given 2,400 mg of Livaux® daily for four weeks. Following treatment, the participants reported a significant increase (P = 0.009) of 0.84 additional bowel movements per week compared to no treatment. In a sub-group of responders[1], this increased to an additional 1.4 bowel movements per week (P = 0.001). Stool form remained healthy with an average Bristol Stool Score of 3.62[2].

CytoSolve In Silico Study

Anagenix commissioned a study through CytoSolve to investigate how Livaux® affects gut motility by way of computer modelling (*in silico* analysis). As part of this study, it was found that the bioactive components within Livaux® support healthy gut motility by affecting three major physiological processes:

- Mucus production
- Control of inflammation
- Faecal bulking

Mucus production

Mucus serves as a protective barrier for the gut lining and as a lubricant to facilitate the passage of stool. Maintaining a thick layer of mucus is therefore important for allowing stools to pass freely and protect against infection.

Livaux® contains the amino acid, leucine, which directly targets the mucus production pathway, stimulating the production of mucin 2, thereby helping to maintain the mucus layer.

Control of inflammation

Two key pathways involved in the inflammatory response are the oxidative stress pathway and TNF-α induced nitric oxide (NO) synthesis from inducible nitric oxide synthase.

Livaux® contains key bioactives which influence these inflammatory pathways, namely vitamins E, A and C and the polyphenol, epicatechin.

Using the CytoSolve computer model, a daily dose of Livaux® was found to reduce both reactive oxygen species (by-product of oxidative stress) and inducible NO production, indicating that Livaux® is able to help control inflammation.

Faecal bulking

Livaux® contains non-digestible, fermentable components in the form of dietary fibre and polyphenols. These components are fermented by the good bacteria in the gut to produce short chain fatty acids (SCFAs), such as propionate, which stimulate the production of PYY and GLP-1. These compounds increase gut transit time, facilitating the optimal absorption of water and other nutrients to promote healthy stool formation and good faecal bulk.

1. Participants were classified as responders if they showed an increase by at least 1 bowel movement per week over the preceding washout period on at least 1 of the non-placebo interventions.

2. Healthy stool scores 3 or 4 on the Bristol Stool Chart.

Bacillus coagulans BC30

Bacillus coagulans GBI30, 6086 (GanedenBC[30]; BC30) is a safe (FDA GRAS status) and well-studied probiotic strain, with 27 peer-reviewed, published studies to date. It is very stable and has been shown to support the digestive and immune systems.

- Daily consumption of BC30 (1 billion cfu) by older adults (64-80 yrs) led to a significant increase in *F. prau* and an increase in the secretion of IL-10 from LPS-stimulated peripheral blood mononuclear cells (PBMCs), indicating anti-inflammatory activity (Nyangale, et al., 2015).
- BC30 treatment limited the recurrence of *Clostridium difficile*-induced colitis following vanomycin withdrawal in mice (Fitzpatrick, et al., 2012).
- BC30 possesses strong immune modulating properties *in vitro,* exhibiting anti-inflammatory activity via the inhibition of oxidative stress-induced reactive oxygen species (ROS) formation (Jensen, Benson, Carter, & Endres, 2010).
- Even when inactivated, the cell walls of BC30 have been shown to positively support the immune system by inducing T cells, increasing immune-activating cytokines (such as IL-1β, IL-6 and TNF-α) and increasing anti-inflammatory cytokines (such as IL-10) (Jensen, Cash, Farmer, & Keller, 2017).
- In a clinical study, participants were given 500 million cfu of BC30 daily for 28 days. Immune cells taken from the participants were then exposed *ex vivo* to an adenovirus strain or an influenza A strain. T cells, IL-6, IL-8, IFN-γ and TNF-α levels increased following exposure to the viruses compared to baseline measurements, indicating that BC30 can enhance immunological responses to common viral respiratory tract infections (Kimmel, Keller, Farmer, & Warrino, 2010).
- A randomised, double-blind, placebo-controlled study investigated the effect of BC30 on gastrointestinal symptoms in adults with post-prandial intestinal gas-related symptoms (abdominal pain, distension and flatulence). Subjects received either 2 billion cfu of BC30 or a placebo daily for 4 weeks. BC30 consumption lead to improvements in 10 of the 12 variables measured, with a significant improvement in abdominal pain ($P = 0.046$) and a strong trend to improvement with abdominal distension ($P = 0.061$) compared to placebo (Kalman, et al., 2009).

Opportunity to Formulate with Livaux®

Kids Digestive and Immune Health Support

INGREDIENTS	AMOUNT PER 3 G DOSE (G)
Livaux®	0.3
***B. coagulans* BC30**	500 million CFU
Inulin (Beneo Orafti)	0.5
Other ingredients, e.g. natural sweeteners	

The formulation is designed around a 3 g single-serve sachet, however could be used in a multiple-serve pack, such as a pouch or tub.

Disclaimer: all formulations in this booklet are concepts only. The receiving party is solely responsible to ensure that all applicable laws and regulations for the intended use of the formulations are duly regarded.

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Anagenix Ingredients
Formulations

Livaux®

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Science

Livaux® is clinically proven to be a novel, targeted prebiotic, boosting the numbers of the beneficial gut bacteria, *Faecalibacterium prausnitzii (F. prau),* by more than 100%. A daily dose of Livaux® also improves bowel regularity.

Key benefits/features

- High quality freeze-dried powder
- Derived entirely from non-GMO New Zealand gold kiwifruit
- No added sugars or preservatives
- Self-substantiated GRAS (Generally Recognised As Safe)
- Pleasant gold kiwifruit flavour
- Multiple format applications
- Recommended daily dose 600 – 2,400 mg

Product concept summaries

Livaux® for microbiome balance

Livaux® is a novel, targeted prebiotic and is therefore useful for microbiome balance. Livaux® tastes great so can be readily used in a ready-to-mix powdered drink. A 600 mg dose will also fit into a size 00 capsule.

Active ingredient(s)	Livaux® (600 mg)
Other ingredients	Dextrose, maltodextrin, xanthan gum (for sachets)
Health application	Digestive health, microbiome balance
Target group	Adults, particularly those with digestive disorders/microbiome dysbiosis (e.g. IBS, IBD)
Suggested dosage forms	Sachet, scoop, capsule
Daily portion	3 g – sachet/scoop 1 – 4 600 mg capsules

Livaux® for immunity

It is well known that the gastrointestinal system plays a significant and central role in the immune system. Livaux® has been shown in a clinical study to support healthy bowel regularity and increase the abundance of the beneficial gut bacteria, *Faecalibacterium prausnitzii,* which in turn helps to support a healthy immune system. The inclusion of vitamins C and D gives the immune system that extra boost that may be needed, for example, over the winter months.

Active ingredient(s)	Livaux® (600 mg) Vitamin C (85 mg – 100% RDA) Vitamin D3 (15 µg – 100% RDA)
Other ingredients	Dextrose, maltodextrin, xanthan gum
Health application	Immunity
Target group	Adults, including elderly
Suggested dosage forms	Sachet, scoop
Daily portion	3 g – sachet/scoop

Livaux® for kids – digestive and immune health support

A lot of kids suffer from digestive discomfort and/or need a boost for their immune system. Livaux® provides key bioactives from gold kiwifruit to support digestive health (through improving bowel regularity and feeding the good bacteria) which in turn supports the immune system. The inclusion of a well-studied, shelf-stable probiotic, *Bacillus coagulans* BC-30, provides an additional boost to the digestive and immune systems.

Active ingredient(s)	Livaux® (300 mg) *Bacillus coagulans* BC30 (500 million cfu/dose)
Other ingredients	Maltodextrin, erythritol, inulin, xanthan gum
Health application	Digestive health, immune support
Target group	Children 2 yrs+
Suggested dosage forms	Sachet
Daily portion	1 x 3 g sachet

Antibiotic support

Following a course of antibiotics, the microbiome can become imbalanced. Livaux® is a prebiotic which can restore balance to the microbiome by helping the beneficial gut bacteria, *Faecalibacterium prausnitzii,* thrive. The well-studied probiotic *Bifidobacterium lactis* BI-04 has been shown to support intestinal balance during and after taking a course of antibiotics, as well as ameliorating the side effects of antibiotics, such as diarrhoea, pain and bloating.

Active ingredient(s)	Livaux® (600 mg) *Bifidobacterium lactis* BI-04 (10 billion cfu/dose)
Other ingredients	Dextrose, maltodextrin, xanthan gum
Health application	Digestive health, immune support
Target group	Adults taking antibiotics
Suggested dosage forms	Sachet, scoop
Daily portion	3 g – sachet/scoop

Other suggestions

As a powdered ingredient, Livaux® is well suited to blending with other powdered ingredients and could be formulated with vitamins, minerals, other probiotics, other fruit and vegetable powders, etc.

For more information, please contact Chris Johnson
+64 21 724 008
chris.johnson@anagenix.com
www.anagenix.com

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please contact Chris Johnson

Mobile: +64 21 724 008 | Email: chris.johnson@anagenix.com

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