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SILKE WATKINS, Editor-in-Chief

## A sounder sleep for a healthy body and mind

A soaring workload, a cluster of deadlines and stress that spreads to your private life? No wonder you find it difficult or impossible to sleep at night.

Medical studies support the theory that sleep disorders and stress go hand in hand. Thoughts whirling around like a washing machine spin cycle as soon as you lie down in bed. The main things that prevent people from sleeping soundly – or at all – include worries, fears and stress. But over and above sleep disorders alone, they often trigger other symptoms, like irritability, fatigue and lethargy. Here, too, we can trace these complaints back to stressful situations and tension.

Statistics from the German Sleep Society show that sleep disorders caused by professional and private stress affect 20 to 30 % of adults regularly. Meanwhile, 10 % report less than restful sleep, either frequently or permanently. A lack of sleep or sleep disorders in general are detrimental to health. They impair performance, concentration and responsiveness and can also spawn mental disorders like depression. Noise and working unsocial hours are other factors that adversely affect healthy sleep.

Prolonged lack of sleep not only harms body and mind, it also weakens the immune system. Normally speaking, evenings should see stress hormones decline and melatonin increase as prerequisites for an immune system in good working order. The weaker this system, the more prone to infections you are. This, in turn, can exacerbate what should be innocuous diseases into something more serious.

Sleeping sufficiently and well isn't just a must for your physical recovery – it's just as crucial for the brain too. Above all for children, sleep is key to anchoring the insights they have learned and ensuring their healthy growth.

These examples illustrate how the various interconnected factors also influence each other.

All these and other topics are included in this issue of Wellness Foods & Supplements.

I wish you an interesting read!

Silke Watkins



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Cover Photo®: Indena S.p.A.

Berberidaceae, the barberry family of the buttercup order (Ranunculales), comprises 14 genera and 701 species of perennial herbs and shrubs. In the Berberidaceae family, the genus *Berberis* comprises of around 450–500 species, which represent the main natural source of berberine. Berberine is a plant alkaloid with a long history of medicinal use in both Ayurvedic and Chinese medicine. Among the various species of *Berberis* genus, *Berberis aristata* DC is one of the most important species due to its wide medicinal properties. It has been used in traditional medicine for its antimicrobial, antiprotozoal, antidiarrheal and antitrichoma activity. (see Cover story at page 6)

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## Indena BERBEVIS®: the natural way to keep the metabolism balanced

### Berberine, a natural treasure for human health

Berberidaceae, the barberry family of the buttercup order (Ranunculales), comprises 14 genera and 701 species of perennial herbs and shrubs. (1) In the Berberidaceae family, the genus *Berberis* comprises of around 450–500 species, which represent the main natural source of berberine. Berberine is a plant alkaloid with a long history of medicinal use in both Ayurvedic and Chinese medicine.

Among the various species of *Berberis* genus, *Berberis aristata* DC is one of the most important species due to its wide medicinal properties. It has been used in traditional medicine for its antimicrobial, anti-protozoal, antidiarrheal and antitrichoma activity. (2)

Berberine is a quaternary ammonium salt derived from isoquinoline alkaloid and it is supported by reliable scientific literature proving its health benefits in multifactorial conditions, including the support in controlling healthy blood levels. (3) The berberine alkaloid can be found in the roots, rhizomes, and stem bark of the plants.

Specifically, berberine's proven effectiveness in the management of multifactorial conditions is related to its so-called “Cloud Effect”: its pleiotropic effect simultaneously targets both root causes (e.g. low-grade chronic inflammation, oxidative stress, gut microbiota modulation) and marks (e.g. insulin levels) through the modulation of several cellular targets (e.g. AMPK, mitochondria, insulin-receptor, key metabolic and pro-inflammatory enzymes, etc.). This helps optimize peripheral blood metabolic profiles by modulating plasma sugar, insulin and lipids levels, thus resulting as a precious resource for the metabolic wellbeing. (4)

### BERBEVIS®, Indena's next generation Phytosome®, to face the challenge of berberine's poor bioavailability

Like many natural compounds, berberine has a poor bioavailability. For this reason, high dosages are traditionally recommended for berberine, that means low tolerability and gastrointestinal side effects. To face such issue, Indena developed since years Phytosome®, the proprietary biomimetic strategy for the delivery of natural ingredients,



allowing human body to absorb them in the best possible way. It is a fundamental asset, and an internationally recognized scientific reference for the delivery systems of natural active ingredients. Phytosome® combines food-grade sunflower lecithin with botanical and natural substances maintaining the original components' profile and benefits. Numerous scientific studies have proven that Phytosome® system delivery offers optimized human pharmacokinetic profiles and effectiveness compared to non-formulated equivalent compounds.

Working on berberine, Indena developed BERBEVIS®, a new and innovative Phytosome® composition, which includes both pea proteins, as a natural vegetable protein carrier, and a powerful, natural antioxidant such as grape seed extract to optimize BERBEVIS® tolerability profile (5).

Remarkably, a human pharmacokinetic study has confirmed that BERBEVIS® has optimized berberine bioabsorption, fostering the substance's bioavailability on molar basis and with observed dose linearity (6). In vitro studies have also shown that Phytosome® formulation enhances berberine solubility in gastrointestinal fluids; has a better bio-accessibility than unformulated *Berberis* extract, improving the amount of berberine released into the gastrointestinal tract and available for absorption; has a higher safety profile than unformulated *Berberis* extract with the absence of negative impact on intestinal membranes. BERBEVIS® appears then to be suitable for a long-term administration.

### **BERBEVIS®: the natural way to keep the metabolism balanced**

It's known that berberine has a multiple mechanism of action on multifactorial conditions. With the aim for the first time to measure the whole range of marks modulation, BERBEVIS® has been used to

supplement the diet of subjects enrolled in a human study focused on PCOS (Polycystic Ovary Syndrome), a complex, multifactorial, endocrine-metabolic disorder.

Clinical evidences show that BERBEVIS® supplementation is the winning multi-target approach to metabolic health maintenance: it optimizes insulin levels effectively and noticeably modulates the blood sugar profile, optimizing both blood glycaemia and insulin. Moreover, a favourable safety profile was reported, with no major adverse events.

As secondary endpoints, BERBEVIS® effectively supports metabolic health, having a positive effect on blood lipid profile, body composition and fostering the redistribution of adipose tissue even in subjects who are not following a low-calorie diet; it promotes hormonal balance, has a positive effect on low-grade chronic inflammation, and it's also helpful for healthy skin, being acne a typical condition of PCOS highly affecting quality of life (7).

All in all, BERBEVIS® is a potent, natural health-food ingredient that might help blood sugar control in a plethora of multifactorial challenges, which represent one of the greatest global health issues of our time.

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## How Robuvit® can help with mood swings, unrefreshing sleep, stress and fatigue

Dr. Franziska Weichmann

In prehistoric times, stress helped our ancestors focus on danger. By increasing the heart and breathing rate, by releasing hormones like adrenaline and by providing more blood and oxygen to the muscles and less to the digestive tract, stressful situations prepared the body for a “fight or flight” response. Nowadays, we react in a similar way when under pressure at work or feeling insecure when facing life changes or traumatic events. Such stressful situations can trigger – or worsen existing – disorders, diseases or pathological conditions (1). Several cognitive functions, like memory or learning capability are negatively affected by chronic stress (1). Stress over a long period can also impair immune system, cardiovascular health, gastrointestinal tract and hormonal balance (1). Furthermore, stress is a risk factor for mood disorders such as burnout syndrome, depression, chronic fatigue syndrome or post-traumatic stress disorder (PTSD) (2). Psycho-physical stress experienced during post-disease or surgery convalescence can have similar consequences.

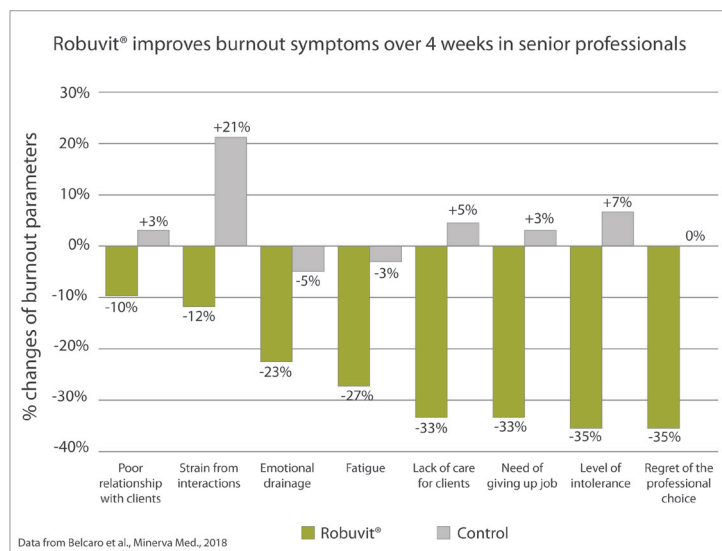
Robuvit®, a standardized extract of French oak wood and a registered trademark of Horphag Research has been shown to help people to better deal with stressful situations, mood changes and resulting fatigue (3–15).

### Dealing with burnout and work-related stress

Burnout occurs in work environments with a continuously high level of stress in a culminating way. This condition comprises emotional exhaustion and decreased sense of personal accomplishment (16). Robuvit® was given to people suffering from burnout syndrome due to particularly stressful circumstances (3). The study comprised surgeons in training as well as senior professionals and managers. Their burnout symp-



toms were assessed by a survey form, including satisfaction at work, level of intolerance, emotional drainage and fatigue. After four weeks of daily Robuvit® intake, the burnout symptoms were significantly relieved in comparison with the control participants.



In a newly published study, nurses under high professional stress took Robuvit® for 4 weeks (4). Burnout in the health care system is a common problem, with 10–70 % of nurses and 30–50 % of physicians and assistants affected (16). The COVID-19 pandemic has exacerbated this phenomenon (17). Supplementation with Robuvit® led to a significantly higher ability to deal with long hours and pressure at work. In addition, participants to the study showed an improved attitude and ability to deal with their working environment, with punctuality and respect towards their colleagues. The desire for self-improvement and interest in learning new skills were ameliorated as well after Robuvit® intake.

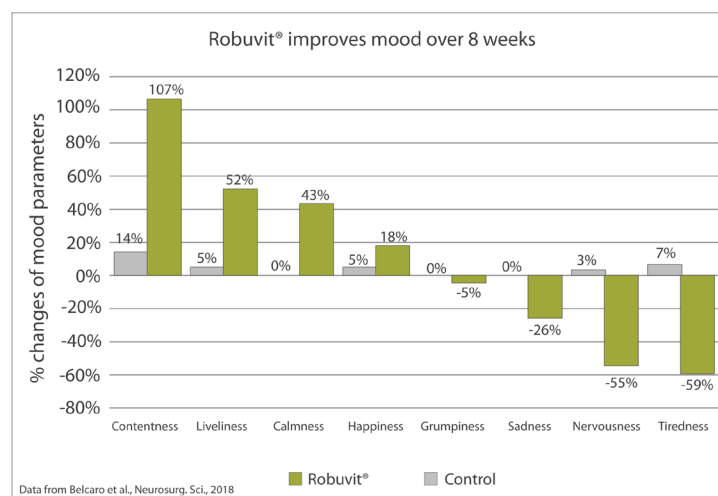
### Improved symptoms of post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) is a very severe form of a psychological trauma that can last for months or even years, if left untreated. Traumatic events such as but not limited to natural disasters, accidents, pandemics, loss of loved ones, combat, or assault can induce nightmares, flashback, anxiety, depressed mood and fatigue (18). In a clinical trial, Robuvit® was supplemented for 4 weeks to patients, suffering from PTSD. Robuvit® was able to reduce the percentage of subjects suffering from recurrent nightmares, memories and intense emotional distress, improved sleep and reduced fatigue (5).

### Reduced fatigue and insomnia

A clinical study investigated the effect of 300 mg Robuvit® per day on energy levels, excluding any other flavonoid consumption. After 4 weeks, the healthy participants stated a significant improvement of energy by 8.8 % as well as a significant reduction of tiredness by

12 % (6). The individuals further reported an improved calmness level, and their motivation in addition they felt less stressed. Another study with 40 individuals, suffering from fatigue, insomnia and mood alterations showed a clear improvement of the indicated conditions, compared to control participants, after taking Robuvit® for 8 weeks. The supplemented subjects had significantly improved mood, felt fitter in the morning with no fatigue during the day and stated to have slept 33 % more (7).



One of the most debilitating forms of tiredness is chronic fatigue syndrome. People that suffer from this not yet fully understood disorder report from persisting tiredness and exhaustion, non-refreshing sleep, muscle and joint pain, dizziness and difficulties with memory and concentration (19). In addition, mood and anxiety disorders are more prevalent in people with chronic fatigue disorder than in people without (20). In a study with patients who suffer from chronic fatigue syndrome, it was shown that Robuvit® could relieve some of these symptoms. After 4 weeks of regular Robuvit® intake, signs and symptoms of bad mood and fatigue were significantly alleviated, compared to the control group, and the energy level was increased by 48 % (9). Another study with subjects with chronic fatigue syndrome for 6 months of daily supplementation with 300 mg Robuvit® confirmed these positive effects (8). Unrefreshing sleep was significantly reduced by 44 %, compared to an increase by 13 % in the control group. Problems with short-term memory was reduced by 29 % and the mood of the participants, taking Robuvit® was significantly improved with a 58 % reduction of depressive feelings and 49 % less mood swings. The control patients showed minimal effects or even slight deterioration.

Patients with mild heart failure also suffer from increased chronic fatigue. A study showed that patients with fatigue due to their mild heart condition was relieved by 58 % after Robuvit® supplementation for 12 weeks, compared to 7 % in the control group, as assessed by the modified fatigue impact scale (10).

A less severe and more self-inflicted problem that includes fatigue and weakness is hangover. Robuvit® was given to people with acute hangover. After 12 hours, the Robuvit® group was significantly less

fatigued, less weak and showed less problems with pain (11). The evaluation of the global mood, including depression, anxiety and irritability showed significant improvement by 55% with Robuvit® compared to an improvement of 28% in control patients.

One last study that was investigating the effects of Robuvit® on fatigue and energy levels was a study, done with men in their fifties and sixties with problems regarding vigor (12). The number of people suffering from lethargy, weakness, inactivity and laziness levels decreased. On the other hand, their energy levels, enthusiasm, verve, mental vitality and even erectile function increased over the 4 weeks of regular supplementation, as evaluated by the participants.

### Improved recovery and convalescence after disease or operation

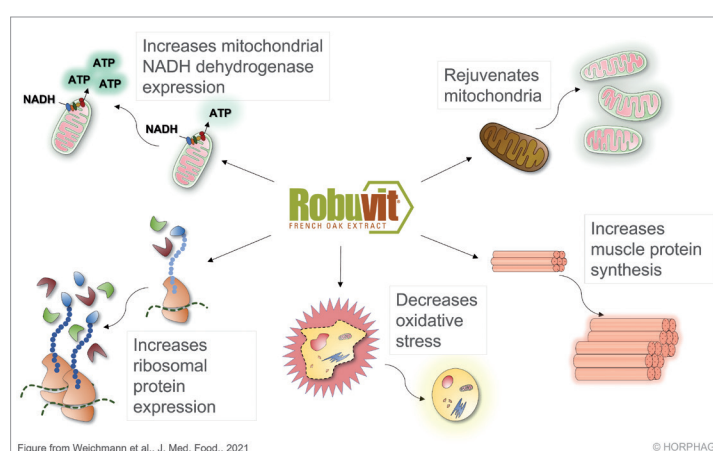
Physical health conditions following surgical interventions or viral infections are very often associated with fatigue and mood swings. Robuvit® was given to patients after they had an operation or a disease, with the effect of increased energy levels and improved recovery (13–15).

A recent study investigated the effects of Robuvit® on patients, recovering from hysterectomy (the surgical removal of the uterus) (13). The women started the supplementation 3 days after the surgical intervention. The group that took Robuvit® for 4 weeks showed significantly improved mental and general health compared to placebo controls by 12 and 18%, respectively. The energy levels of the women of the Robuvit® group increased by 3%, compared to a decrease of 10% in the placebo group. The investigators suggested that Robuvit® can be used to relieve post-operative symptoms, particularly including mental health problems. In another study, patients after having had acute flu symptoms were followed for 3 weeks, taking Robuvit® (14). The Robuvit® subjects stated to have improved signs of convalescence. This includes, among other parameters, a 25%-reduced level of weakness compared to control patients, a 24%-improved sleep pattern than the control patients indicated and around 50% higher attention and concentration abilities than control subjects. Overall, patients in convalescence of a viral disease were shown to have benefits regarding energy and attention, when taking Robuvit®. Another viral disease that commonly leads to long lasting fatigue is infectious mononucleosis, transmitted through the Epstein-Barr virus. In an intervention study, the effects of 4 weeks of Robuvit® supplementation on mononucleosis recovery were evaluated (15). Fatigue, general feeling of unwellness and body aches were reduced significantly after Robuvit® supplementation compared to control patients.

### Mechanisms of Robuvit® to improve mood and stress levels

Robuvit® has been shown to increase the energy capacity of individuals in several clinical studies (21). Robuvit® metabolite Urolithin

A can lead to an increased generation of new mitochondria (22). Mitochondria are the powerhouses of the cell, where the sugar that we eat gets converted into adenosine triphosphate (ATP), providing energy to drive many processes in cells. In addition, Robuvit® helps improve energy by increasing the number of produced ribosomes (23). Ribosomes are responsible for the production of new proteins, needed for generating messenger hormones, enzymes, muscle fibers and others, including signaling proteins needed to fight during challenging mental health conditions. Furthermore, inflammation was suggested as being involved in the development of mood and anxiety disorders (24). Robuvit® supplementation was shown to decrease inflammatory marker CRP in the blood of patients by 64% compared to a 39% decrease in control patients (25). Additionally, as inflammation and oxidative stress are very closely related pathophysiological processes, the antioxidant capacity of Robuvit® shows to be helpful in this context as well (26, 27).



Robuvit® is an oak wood extract that helps to manage mood problems and stressful situations. These effects were shown in clinical studies in several patients, suffering mood swings, fatigue, burnout syndrome and subjects in convalescence. The results show that Robuvit® helps people handling demanding and frustrating situations better while improving their overall energy and their mood.

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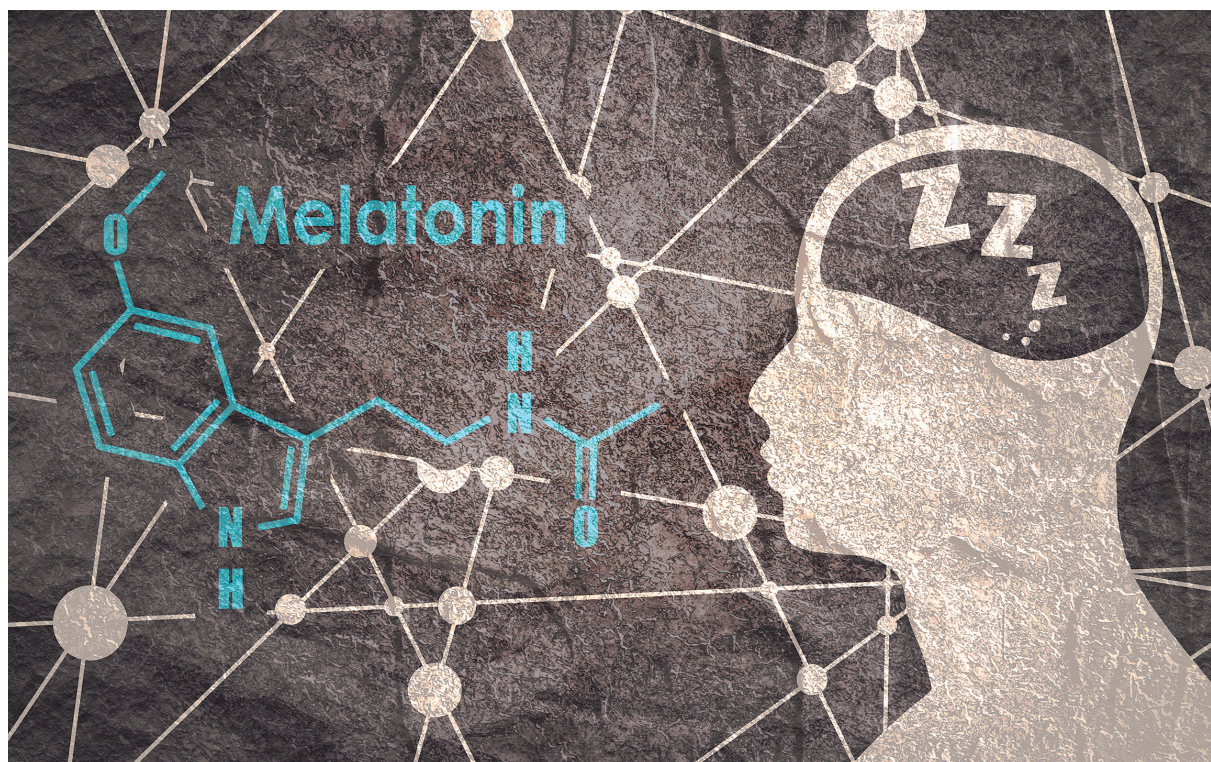


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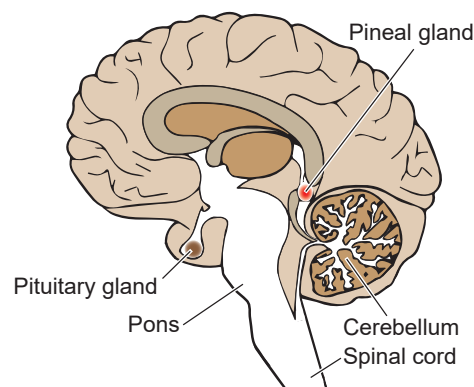
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## Melatonin – a versatile substance not only for sleep disorders

Philipp Gebhardt

Melatonin is a hormone synthesized and released by cells in the pineal gland. It controls the day-night rhythm of the human body and promotes sleep. The European Food Safety Authority (EFSA) considers it scientifically proven that melatonin helps to alleviate the subjective sensation of jet lag and to reduce the time it takes to fall asleep. Melatonin also has endocrine effects and affects the functioning of the immune system. Current scientific studies have shown positive effects on various diseases.

The endogenous hormone melatonin is formed from serotonin by the pineal cells of the epiphysis (Fig. 1). Melatonin synchronizes the organism to the 24-hour rhythm of day and night. The synthesis and release of the hormone are stimulated by darkness. The blood concentration increases during the night, the maximum is reached around three o'clock in the morning (Fig. 2). In children, values can be measured about twelve times higher at night than during the day. With increasing age, less melatonin is formed (Fig. 3). Melatonin is a natural antagonist of the stress hormone cortisol. Reduced melatonin formation is associated with sleep disorders or disorders of the sleep-wake cycle. (1)



*Fig. 1: Melatonin is formed from serotonin in the epiphysis located in the diencephalon. The activity of certain enzymes involved in melatonin synthesis is indirectly dependent on daylight.*

### Melatonin in insomnia

Sleep is vital for the regeneration of body and mind. A good and restful sleep is important for our daytime well-being and our perfor-



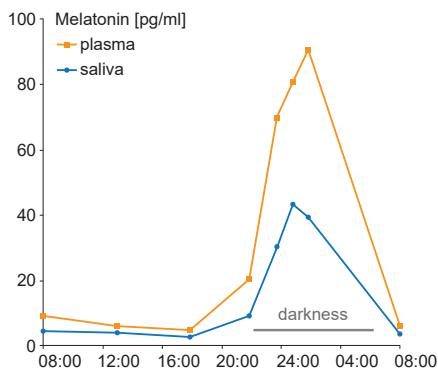


Fig. 2: The synthesis of melatonin is inhibited by light and stimulated by darkness. The highest concentrations are reached around midnight. During the second half of the night, the concentrations fall off. (2)

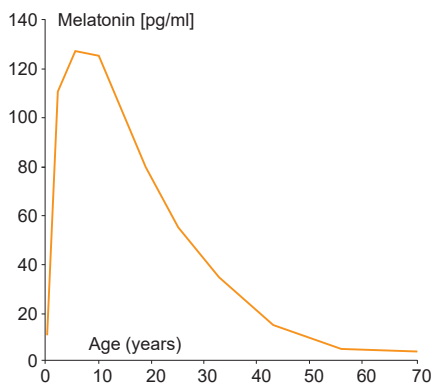


Fig. 3: The formation of melatonin varies with age. The highest concentrations are reached during early childhood. With increasing age, less melatonin is produced. From the age of about 55 years, only low levels can be measured. (2)

mance, both mentally and physically. Sleep is also very important for learning. During sleep, processes take place that consolidate what has been learned. Sleep disorders lead to reduced performance and tiredness during the day, irritable mood and disturbances in attention and concentration. According to this, about 10% of adults in industrialized countries suffer from chronic insomnia symptoms, which are characterized by difficulty falling asleep, sleeping through the night or only superficial and non-restorative sleep. (3) It has been proven that sleep disorders impair the function of the immune system and increase the risk of heart attacks, heart failure and high blood pressure in the long term.

Due to its chronobiological effect, melatonin is being studied for the treatment of sleep disorders and as a natural sleep aid. According to a review that evaluated the data of 1,683 participants, melatonin can contribute significantly

to reducing the time it takes to fall asleep as well as increasing sleep time. Longer use and a higher dosage were associated with greater effects. The use of melatonin also led to a significant improvement in sleep quality. (4) It has also been shown that melatonin can reduce disturbances in the sleep-wake cycle after long-haul flights (jet lag). (5) In clinical practice, melatonin has also proven itself as a suitable substance for inducing sleep in children with psychomotor disorders. Significant improvements in terms of sleep duration and sleep quality could be demonstrated. (6)

### Melatonin as an antioxidant

As highly reactive intermediate products of the metabolism, free radicals damage the body's own tissues. It is assumed that corresponding damage to the DNA can also lead to degenerative diseases or cancer. Melatonin forms a direct radical scavenger for oxygen and nitrogen radicals, which is characterized by the fact that the resulting metabolites can also neutralize radicals. This property is called a cascade reaction and makes melatonin a particularly potent antioxidant. In addition, melatonin seems to significantly improve the body's antioxidant capacity, as it positively influences both the cellular formation and the activity of antioxidant enzymes. (7)

### Effect on the mitochondria

Mitochondria are cell organelles in which the oxidative phosphorylation, the generation of energy with oxygen consumption, takes place. The number of mitochondria per cell is typically in the order of 1000 to 2000, with a volume fraction of about 25%. While 2 moles

of adenosine triphosphate (ATP) per mole of glucose can be obtained through anaerobic fermentation, aerobic energy generation via the respiratory chain located in the mitochondria enables 36 moles of ATP per mole of glucose. Due to the high efficiency of oxidative phosphorylation, more than 90% of the organism's energy is formed in the mitochondria. Since ATP cannot be stored in significant amounts, it has to be constantly regenerated from ADP in the cells. The daily conversion of ATP is in the range of a person's body weight. Mitochondria are believed to have been incorporated into more developed cells during evolution as bacterial symbionts. Mitochondria have their own genome, which is sensitive to oxidative damage due to its simple structure. Damage to the mitochondrial genome results in reduced energy production and is associated with the increased occurrence of chronic diseases in old age.

Melatonin concentrations are about 100 times higher in mitochondria than in plasma. (8) Melatonin plays a special role in the mitochondria because it protects a special phospholipid, cardiolipin, from reactive oxygen radicals. (9)

Cardiolipin is the only phospholipid synthesized exclusively in the mitochondria. It is stored in the inner mitochondrial membrane and serves to stabilize the respiratory chain complexes. According to recent findings, cardiolipin helps to give the membrane a specific shape, which is also required for the efficient functioning of a transport protein called Aac2. Aac2 transports ADP into the mitochondria and ATP out of the mitochondria (Fig. 4). (10)

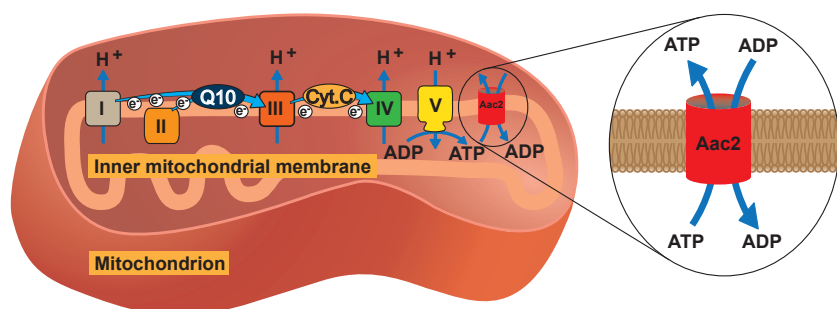


Fig. 4: Mitochondria are cell organelles enclosed by a double membrane. The inner membrane carries the respiratory chain complexes. These are proteins that catalyse oxidative phosphorylation, the production of energy while consuming oxygen. The transport protein Aac2, which transports ADP into the mitochondria and transports ATP out of the mitochondria, is also stored in the inner membrane.

Accordingly, for example, an interruption in the blood supply or the restoration of blood flow to tissues that have not been supplied with blood or only insufficiently supplied with blood for a certain period of time leads to increased oxygen radical formation in the affected mitochondria and to oxidative damage to cardiolipin. (11)

Corresponding damage occurs after strokes, heart attacks or vascular surgery. In this context, melatonin supplementation can reduce the severity of the so-called reperfusion damage. (12)

### Melatonin in cancer

Melatonin is also being studied for its anti-cancer properties, as low levels of melatonin are associated with an increased incidence of certain cancers. (13) In addition to its antioxidant effects, melatonin modulates oestrogen and androgen activity, has an immunomodulatory effect, and inhibits the growth and proliferation of cancer cells. (14) A meta-analysis on complementary cancer therapy showed a 33 % lower mortality rate after evaluating the data of 643 study-participants, without melatonin intake being associated with significant side effects. (15) A similar result was confirmed in a more recent review with 3,697 participants. (16) It could also be shown that supplementation can significantly reduce fatigue as a result of cancer or chemotherapy and radiotherapy. (17)

### Melatonin in type 2 diabetes mellitus

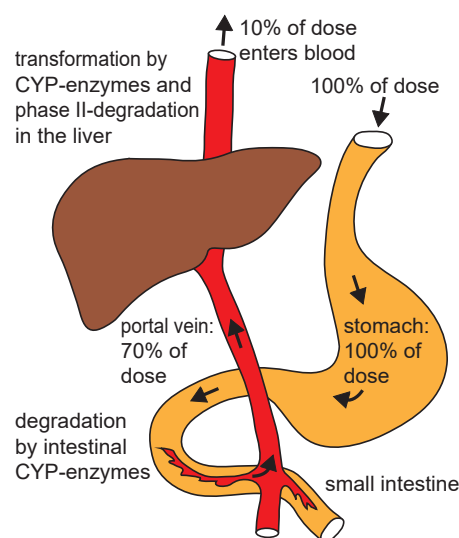
About 90% of diabetes cases can be assigned to diabetes mellitus type 2. In contrast to type 1, which is based on an absolute lack of insulin, in type 2 insulin is still present, but it cannot work properly on the receptors of the target cells (insulin resistance). Since the absorption of glucose from the blood into insulin-dependent cells is inhibited, there is a lack of energy in the appropriate tissues. The concentration of glucose in the blood is elevated. As a result, sugar increasingly reacts with endogenous proteins, resulting in so-called glycosylation products. A glycosylation product of haemoglobin, the so-called HbA1c, is used in diabetic patients as a marker for the quality of blood sugar control over the last 8–12 weeks. The glycosylation products are broken down by the immune system, resulting in inflammatory reactions with increased formation of oxygen radicals. This sets the stage for macro- and microvascular damage leading to the complications of the disease. (18) In Germany, the prevalence of type 2 diabetes mellitus among 55–74-year-olds is in the range of 15%, so that in this age group almost every seventh person is affected by the disease. It is assumed that the number of diabetics will continue to increase.

Compared to healthy people, melatonin production is reduced in type 2 diabetics. It was shown that melatonin can have a positive effect on certain blood levels in those affected. In a study, 64 type 2 diabetics received 6 mg of melatonin each day. After six weeks, significantly lower blood sugar levels and HbA1c values could be measured in the participants compared to taking a placebo. Levels of high-density

lipoprotein (HDL), which transports excess cholesterol from blood vessel walls back to the liver, also increased significantly. (19) A similar study was also able to show that melatonin can contribute to lowering the blood pressure in diabetic patients. (20) Beneficial effects on the blood sugar level, the HbA1c value and the severity of the insulin resistance could also be confirmed in a review article. According to this, a dietary melatonin supplement can significantly improve certain blood values of type 2 diabetics. (21)

### Increase in bioavailability through liposomes

Melatonin is also found in plant foods like cranberries, pistachios, and cherries. In this form, however, the active ingredient is only available to a small extent for most organs. Like melatonin taken in the form of capsules or tablets, it is absorbed from our food in the small intestine and reaches the liver via the portal vein. In the liver, the major part of the active substance is degraded. As a result, only a small part of the ingested dose can be distributed in the body (Fig. 5). A modern alternative with significantly better bioavailability is offered by so-called liposomal formulations, which contain the active ingredient in tiny droplets covered with a double layer of



*Fig. 5: Melatonin is already oxidized by CYP enzymes in the intestine and thus broken down. Further biotransformation takes place by CYP enzymes and conjugation reactions in the liver. Most of the absorbed dose is rendered ineffective during the first passage through the liver ("first-pass effect").*



phospholipids. Phospholipids are a natural component of bile that improves the absorption of nutrients. Melatonin supplied in liposomal form can be absorbed much better in the small intestine. However, a relevant part of the active ingredient is already absorbed through the oral mucosa, so that the passage through the liver via the portal vein is bypassed and a significantly larger part can reach the organs of the body. Because of its good bioavailability, liposomal melatonin is particularly recommended.

## Conclusion

Although the sleep-inducing effect of melatonin is not comparable to the effectiveness of a pharmacological treatment, the active substance is particularly suitable for therapeutic use since no serious side effects are to be expected. In insomnia, the effect should set in after two to three weeks with regular use. If the sleep disturbances persist after this time, cognitive behavioural therapy or drug therapy under medical supervision may be necessary. In addition to its use as a natural sleeping aid, studies show promising effects on reperfusion damage, type 2 diabetes mellitus and cancer. Melatonin in the form of capsules or tablets is mostly broken down during the first passage through the liver. Therefore, liposomal melatonin formulations should be preferred as food supplements, because they stand out regarding their good bioavailability. In this form, a relevant amount of melatonin is already absorbed through the oral mucosa, passing by its degradation in the liver. Melatonin should be taken just before bedtime so that it can support the natural sleep-wake cycle.

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## A natural chewing experience: Chewing gum with ERYLITE® Erythritol

Dr Marianne Dölz, Florian Gutschalk, Johanna Guse

The mysterious product chewing gum has fascinated mankind already for centuries. As well as providing a pleasant experience, chewing gum has been shown to have beneficial effects on concentration and cognitive function, as reported in several studies.<sup>[1]</sup> While early forms of chewing gum relied on tree resin (e.g. chicle) and waxes, the development of synthetic gum bases has since enabled the market to flourish and diversify into all sorts of colours, forms, flavours, textures and functions. Nevertheless, the basic principle remains the same: A water-insoluble phase delivers the chewing body, while the water-soluble phase provides sweetness and flavour.

The water-insoluble gum base is a complex matrix of ingredients whose exact composition is usually a well-protected trade secret. Key ingredients include elastomers, solvents, polymers, and emulsifiers, but waxes, plasticisers and fillers also contribute to a unique matrix whose mouthfeel, hardness, stickiness and flavour binding capacity is influenced by the choice and exact amount of each component.<sup>[2,3]</sup> Interestingly, the water-soluble phase can influence the texture of the final product despite being added to a gum base that is already pre-mixed. This phase consists mainly of sweeteners, humectant, and flavours. The amount of the individual ingredients is key, but additionally, the water content of the components or the granularity of the sweetener may influence the hardness of the gum.<sup>[4]</sup> In the case of sugar-free chewing gums, the sweeteners are usually a composition of different polyols combined with high intensity sweeteners to achieve the best possible sweetness profile. This complex combination of ingredients was a challenge for this project.

### ERYLITE® and the growing demand for natural chewing gums

Conventional chewing gums, with matrices based on synthetic polymers such as polyvinyl acetate, cannot be classed as natural products.<sup>[5]</sup> Moreover, synthetic chewing gums of this type are not biodegradable and can leave ugly residues in public places such as pavements, even prompting discussions about a “chewing gum tax” in Great Britain in 2021.<sup>[6]</sup> This, together with the general increase of consumers’ interest in natural ingredients and their awareness of the contents of their food, is opening up new opportunities for natural gum bases. A chewing gum can only be marketed as a natural product if all of its ingredients meet certain criteria, increasing the need for natural sweeteners.

Jungbunzlauer’s ERYLITE® erythritol is a polyol manufactured by fermentation from glucose syrup, which is obtained from maize. Since the fermentation process does not involve genetically modified organisms, and the use of chemicals is avoided during processing, Jungbunzlauer considers ERYLITE® to be a natural sweetener. The idea of using erythritol in chewing gum is not new, but its use was widely patented in the early nineties, significantly restricting the development of new recipes over a prolonged period. However, many of those patents have expired over the past 15 years and all of the major market players have launched chewing gums containing erythritol. The aim of the studies reported in this article was to illustrate the basic functionalities of ERYLITE® as an ingredient of chewing gum.



Erythritol provides only about 60 % of the sweetness of sugar, so high-intensity sweeteners such as stevia need to be added to augment the sweetness in most cases. Even so, the negative heat of solution generated by ERYLITE® makes it an interesting candidate for inclusion in chewing gum. The dissolution of ERYLITE® induces a cooling effect in the mouth, which pairs well with mint flavours. We decided to use xylitol as a reference polyol for our experiments, because it demonstrates a similar cooling effect and appeared to exhibit the greatest similarity with ERYLITE® out of all the polyols currently used in the chewing gum industry.

### Development of chewing gum recipes

Two recipes were developed (table 1) using a natural chicle gum base and a synthetic gum base which are commonly used in the confectionery industry. Both of these recipes contain Jungbunzlauer's ERYLITE® in combination with stevia rebaudioside A (RebA) to adjust the sweetness. Jungbunzlauer produces ERYLITE® F8030 granules, with max. 25 % of particles above 800 µm and max. 10 % below 300 µm. However, the ERYLITE® was milled and sieved to obtain the finer particles required for a chewing gum with pleasant mouthfeel and chewing experience. Only particles smaller than 150 µm were used in the recipe.

Table 1: Chewing gum recipe with synthetic and natural chicle gum

Synthetic gum base		
	[g]	[%]
<b>ERYLITE®</b>	<b>610.00</b>	<b>60.65</b>
Stevia RebA	0.732	0.07
Synthetic gum base	300.00	29.83
Maltitol syrup	50.00	4.97
Glycerine 99.5%	15.00	1.49
Lecithin	5.00	0.50
Mint flavour (liquid)	5.00	0.50
Peppermint flavour (solid)	7.50	0.75
Mint flavour (solid)	12.50	1.24
<b>Zinc Citrate Dihydrate*</b>	<b>0.049</b>	<b>0.005</b>
Total	1006	100

Chicle gum base		
	[g]	[%]
<b>ERYLITE®</b>	<b>640.00</b>	<b>63.63</b>
Stevia RebA	0.768	0.08
Natural chicle gum base	300.00	29.83
Glycerine 99.5%	40.00	3.98
Mint flavour (liquid)	5.00	0.50
Peppermint flavour (solid)	7.50	0.75
Mint flavour (solid)	12.50	1.24
<b>Zinc Citrate Dihydrate*</b>	<b>0.049</b>	<b>0.005</b>
Total	1006	100

\*Zinc Citrate Dihydrate or Zinc Lactate were only tested for off-notes in a sensory screening as indicated and not contained in the standard recipe.

As mentioned in the introduction, each of the ingredients in a chewing gum has a specific function and is therefore essential to the composition. Glycerine acts as a moisturiser and prevents the chewing gum from drying out. Maltitol syrup is a sugar-free alternative to glucose syrup. It also serves as a binding agent and plasticiser. Furthermore, it gives texture to the chewing gum. The chicle

gum base is inherently soft and elastic, therefore it was not necessary to add maltitol syrup to the chicle gum. A mixture of liquid and powdered mint flavours provided a pleasant, fresh aroma. The flavourings also function as plasticisers. Lecithin additionally supports the homogenous distribution of the flavour and plasticisers.

Preliminary trials were conducted on the fortification of these two chewing gum products with zinc, using 15 % of the recommended nutrient reference value (NRV) per 100 g product. Jungbunzlauer zinc salts are often used in dental care products such as toothpastes, mouthwashes and chewing gums due to their antimicrobial and anti-inflammatory effects and its ability to reduce or inhibit the formation of dental plaque and tartar. Jungbunzlauer produces zinc lactate and zinc citrate, which differ in terms of mineral content and solubility (zinc lactate is 23 % zinc with a solubility of 55 g/L; zinc citrate dihydrate is 32 % zinc with a solubility of 2.6 g/L). Fortification with minerals may alter the taste of the final product, and this must be taken into consideration when formulating the product. However, the recommended NRV for zinc is very low, thus only small amounts are needed to fulfil oral hygiene benefit claims.

### Production process

Synthetic gum base and maltitol syrup were mixed using a Z-type kneader. One third of the ERYLITE® was added and kneaded for 10 minutes. Another third of ERYLITE® was then mixed in followed by glycerine and the rest of the ERYLITE®. Finally, lecithin and flavour were added.

The chicle-based chewing gum was prepared in a similar way but without the maltitol syrup and lecithin, starting with mixing the gum base and glycerine. One third of the ERYLITE® amount was then added and kneaded for 10 minutes followed by the remaining ERYLITE® and flavouring added at the end. The chewing gum mass was rolled out with talcum to prevent sticking and cut into strips.

For analytical comparison, chewing gums containing xylitol were produced instead of ERYLITE® using a similar procedure.

### Analysis methods for chewing gum

#### Shelf-life test and storage

Chewing gum strips of each recipe were stored unpacked under different climatic conditions (different temperatures and relative humidities (RH)) for two months:

- Temperate condition: Room temperature (21 °C); 40–60 % RH
- Subtropical/Mediterranean condition: 30 °C, 50 % RH
- Hot/humid condition: 30 °C, 65 % RH



Chewing gums can dry out or bind water, which causes them to lose or gain weight and shorten their shelf life. The samples were weighed regularly to document the changes in mass, which are associated with instability.

### Texture analysis

Chewing gums were cut into strips of the same dimensions (40 mm x 15 mm x 2 mm) and pre-heated to 50°C in a climatic cabinet. Shortly before the measurement started, the samples were removed and fixed centrally to a sample platform and hook. Analysis started at 35°C ± 2°C, simulating oral temperature. Once a trigger force of 5 g was attained, the hook was used to extend the chewing gum sample until its elastic limit (at maximum force) was exceeded and the sample broke. At this point, force and distance were noted and used as an indication of chewing gum extensibility. The maximum force required to break the chewing gum into two pieces is expressed as “resistance to extension”. The degree or distance to which a product can be extended before it breaks is referred to as “extensibility” and correlates to the elasticity of a product.<sup>[7]</sup> The texture analysis was carried out ten times per recipe.

### Sensory evaluation

Jungbunzlauer’s internal sensory panel conducted an initial sensory screening of chewing gums using the “just- about-right” (JAR) scale. This provided information on perceptions of texture, sweetness as well as flavour intensity and cooling sensation, and their possible impact on acceptance of the various products. Attributes were evaluated over time starting at 10 seconds and ending after 120 seconds of chewing. Panellists had to evaluate whether the intensity of each attribute is perceived as “just right”, as opposed to either too much, not enough, too soft or too hard.

A further discriminative evaluation (paired comparison tests) was conducted. The panellists directly compared the two versions in terms of hardness, sweetness and cooling effect.

19 to 26 panellists participated in the sensory sessions and the significance level applied for statistical analysis was set at  $\alpha=0.05$ .

Finally, chewing gums to which zinc salts had been added manually were also evaluated for off-notes. Zinc lactate and zinc citrate were mixed into the synthetic-based chewing gum with ERYLITE®. This sensory session with 12 participants took place under informal conditions and expressiveness is therefore limited. Nevertheless, the data provides an initial indication of the impact of zinc salts on the taste of chewing gums with ERYLITE®.

## Results and discussion

### Storage tests

The results of the storage tests are shown in the following graphs. All chewing gums changed weight during the storage time, independently of the gum mass or polyols. The highest mass changes,

ranging from 2.6% to 4.6%, were observed under hot/humid conditions (figure 3). During storage under subtropical conditions (figure 2) and at room temperature (figure 1) mass changes were very small for all samples, with a maximum weight change of 1.75% (chicle gum base with ERYLITE® or xylitol).

Fig.1: Relative mass change of chewing gum with synthetic or natural chicle gum base, sweetened with xylitol or ERYLITE® and stored under temperate conditions

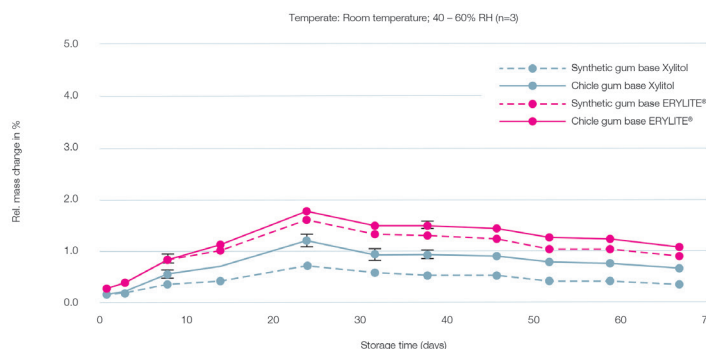


Fig. 2: Relative mass change of chewing gum with synthetic or natural chicle gum base, sweetened with xylitol or ERYLITE® and stored under subtropical/Mediterranean conditions

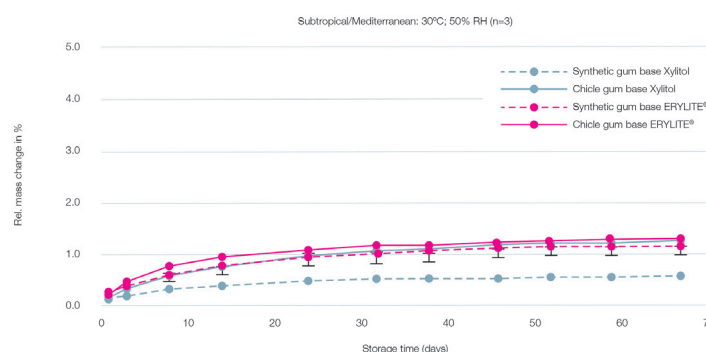
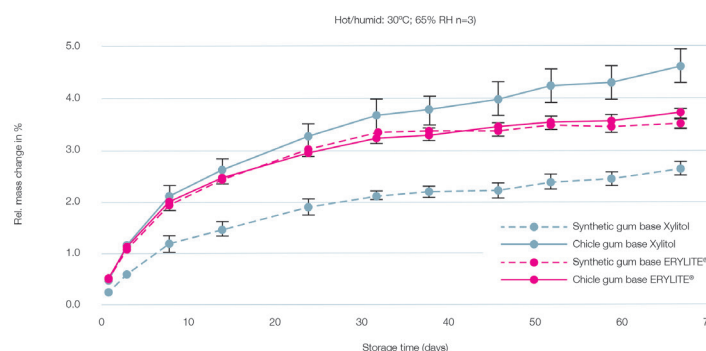


Fig. 3: Relative mass change of chewing gum with synthetic or natural chicle gum base, sweetened with xylitol or ERYLITE® and stored under hot/humid conditions



According to the literature, xylitol is highly hygroscopic while erythritol is not hygroscopic as compared to sugar or other sugar alcohols.<sup>[8]</sup> Nevertheless, the storage tests showed both recipes to be relatively

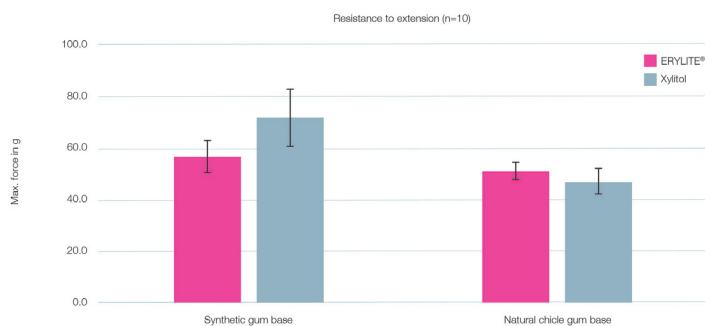


stable at room temperature and under Mediterranean storage conditions. Interestingly, while small differences were observed between the synthetic and the chicle gum base with xylitol under hot/humid conditions, the samples with ERYLITE® exhibited similar behaviour regardless of which gum base was used.

### Texture analysis

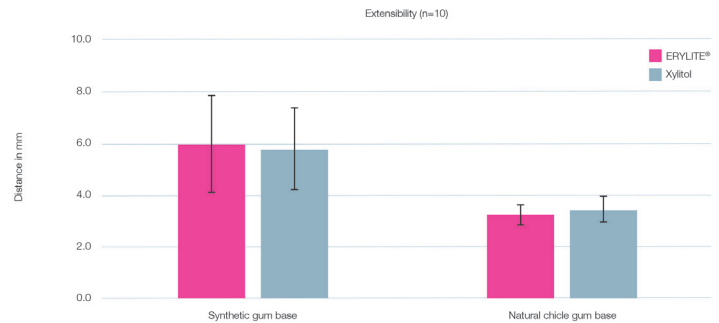
The following figure 4 shows that the force required to break the chewing gums is similar regardless of whether they contain ERYLITE® or xylitol. Although the synthetic gum containing xylitol appeared to be more resistant to extension, this was not statistically significant and ERYLITE® and xylitol are comparable in this respect.

Fig. 4: Resistance to extension of chewing gum with synthetic or natural chicle gum base, sweetened with xylitol or ERYLITE®



The extensibility (figure 5), i.e. the distance until the chewing gums break, is the same for ERYLITE® and xylitol, in combination with both the synthetic gum base and the natural chicle gum base.

Fig. 5: Extensibility of chewing gum with synthetic or natural chicle gum base, sweetened with xylitol or ERYLITE®



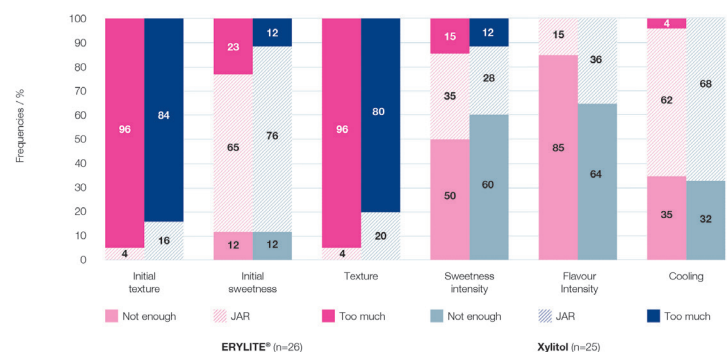
The texture analysis represents an attempt to illustrate the effects of ERYLITE® and xylitol on texture based on quantitative data. Although the method might miss some physiological aspects like the influence of saliva, it provides a good indication that adding ERYLITE® or xylitol will lead to similar effects in each case.

### Sensory evaluation

For the “just-about-right” analysis, each product was evaluated in a separate session on different days and so there was no direct comparison in this set-up. The following graphs show the results expressed as frequencies of each attribute for synthetic chewing gum with ERYLITE® or xylitol as well as chicle gum with ERYLITE® or xylitol.

Both sensory evaluations with chewing gum using the synthetic gum base (figure 6) indicate that the texture of the chewing gum was perceived as too hard, both initially and after 120 seconds of chewing. The initial sweetness was mostly rated “just right” but overall sweetness intensity decreased while chewing. This was especially the case for chewing gums with ERYLITE®. The flavour was not intense enough in either product. The cooling sensation was perceived as “just right” by 62 % (ERYLITE®) and 68 % (xylitol), respectively.

Fig. 6: Results of “just-about-right” analysis of synthetic gums with ERYLITE® and xylitol



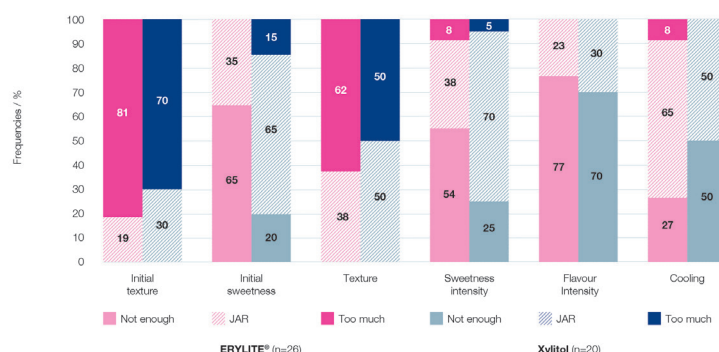
Irrespective of whether ERYLITE® or xylitol was used, both chewing gums with the chicle gum base (figure 7) were perceived as too hard at the initial stage. However, the chicle gum versions were rated as less hard compared to the synthetic gum base.



The initial and overall sweetness of xylitol seems to be higher (“just right”) compared to ERYLITE® (initial sweetness vs. sweetness intensity).

Flavour expression was too low in both chicle-based chewing gums. The cooling sensation was pleasant and with ERYLITE® even more acceptable (65 % “just right”) than with xylitol (50 % “just right”).

Fig. 7: Results of “just-about-right” analysis of natural chicle gums with ERYLITE® and xylitol



Detection of potential differences between the two sweetening systems was enhanced by comparing both versions of synthetic gum and natural chicle gum directly through paired comparison tests for attributes of specific interest (sweetness, hardness and cooling sensation) as shown in table 2.

Table 2: Results of paired comparison tests (n=19, sign. level  $\alpha=0.05$ )

Paired comparison tests	Sweetness	Hardness	Cooling effect
Synthetic gum base: ERYLITE® vs. xylitol	No sign. difference (p-value: 0.3593)	No sign. difference (p-value: 0.0636)	Sign. difference (p-value: 0.0192)
Natural gum base: ERYLITE® vs. xylitol	Sign. difference (p-value: 0.0192)	No sign. difference (p-value: >0.9999)	No sign. difference (p-value: 0.3593)

There was no significant difference between the synthetic chewing gum with ERYLITE® or xylitol in terms of sweetness or hardness. This corroborates the findings of the “just-about-right” evaluation where both synthetic gums were perceived as too hard and overall sweetness values were low. In this direct comparison, the cooling effect was perceived as significantly stronger for the xylitol version.

The chewing gums based on chicle did not differ significantly in terms of hardness or cooling effect, but here xylitol was perceived as signifi-

cantly sweeter than ERYLITE®, which can be also seen in the results of the “just-about-right” analysis (initial and sweetness intensity).

The results of the paired comparison tests complement the findings of the “just-about-right” evaluation and reveal that, in general, there may be differences between ERYLITE® and xylitol. However, no conclusions can be drawn from this study regarding the extent to which these differences are due to the inherent properties of the sweetener or the overall recipe (influence of gum bases or other ingredients).

During the sensory evaluation, some of the panellists were critical of the hardness of the gum during chewing. Since this applied to both polyols, this is most likely to be due to a problem in the underlying recipe and could be resolved with appropriate modifications. A first step would be to address the milling and/or sieving of the particles. Finer sweetener particles generally increase hardness of the gum and therefore, modification of the particle size distribution would improve the texture. Alternatively, the amount or composition of the gum base could be modified using plasticisers and moisturisers. A second criticism was the sweetness, which was perceived as less pronounced in the chewing gums with ERYLITE®. Here, we suggest increasing the amount of stevia. In any case, producers will develop a recipe that provides their desired final texture, flavour and sweetness intensity.

Finally, an informal sensory screening comparing chewing gums with and without zinc salts indicated that Jungbunzlauer zinc salts do not seem to have a negative impact on taste. However, since these results were obtained only with a small test panel and the addition of only 15% NRV in 100 g of chewing gum, further experiments and testing are recommended.

## Regulatory

Both erythritol and xylitol are Group IV polyols. They can be used quantum satis in chewing gums provided that the product recipe contains no added sugar (Commission Regulation (EU)





No 1129/2011). In the US, erythritol and xylitol both can be used up to 75% in chewing gum.

We would also suggest conducting a careful evaluation of local regulatory restrictions of mineral fortification in sweets. This is generally allowed in Europe, but restricted by the FDA.

## Summary

In conclusion, our results show that ERYLITE® can be used as a sweetener in chewing gums and offers a natural alternative to other commonly used sweeteners. Results for recipes with ERYLITE® were very similar to those with xylitol in terms of storage stability and texture analysis. Some differences that were detected during the sensory evaluation can be addressed easily by making adjustments to the recipe.

## Acknowledgements

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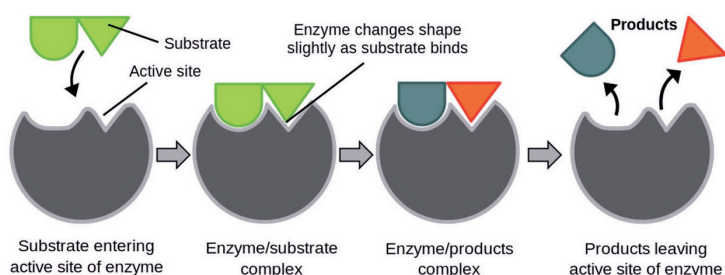


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## Actinidin: A natural protease from kiwifruit

### What are enzymes, and more specifically, proteases?

Enzymes speed up biochemical reactions which occur in living organisms, for example, the digestion of food or synthesis of DNA. Enzymes have different functions which are determined by their shape and the type and sequence of amino acids they are made of, and an enzyme will only catalyse the reactions of the specific substances it was made for.



The most commonly known enzymes are our digestive enzymes: lipases, amylases, and proteases. Proteases catalyse the breakdown of proteins (a process known as proteolysis) into smaller protein fragments (called peptides) or into single amino acids. They do this by cleaving the peptide bonds between the amino acids making up the protein. In the body, the breakdown of dietary protein is essential as it allows for the absorption of amino acids into the bloodstream. These amino acids can then be distributed through the rest of the body, usually to be utilised as building blocks by cells in the body to create new proteins, such as enzymes, antibodies, structural proteins (e.g., keratin, collagen



and elastin), and messenger proteins (e.g., hormones). Muscles and tendons are predominantly protein, which is why bodybuilders supplement their diets with protein or amino acids.

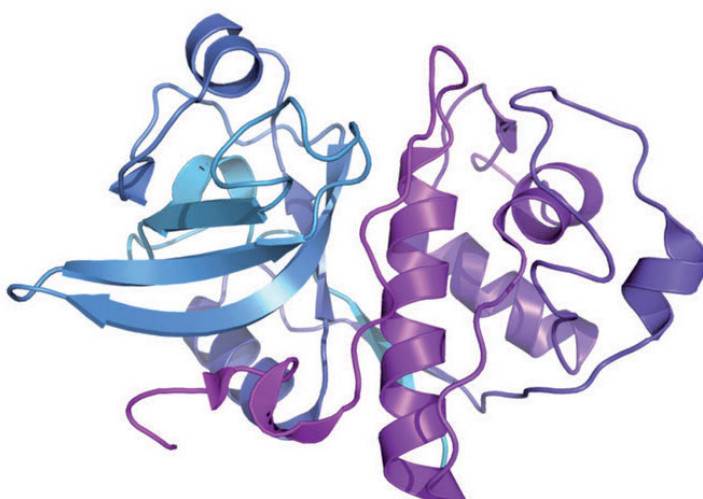
Proteases can be classified into various groups, depending on the amino acid(s) the protease utilises in its active site for proteolysis. Cysteine (or thiol) proteases are one such group (i.e., it contains the amino acid cysteine in its active site) and are commonly encountered in fruit, including papaya (papain), pineapple (bromelain), fig (ficin) and kiwifruit (actinidin). In contrast, our natural stomach protease (pepsin) is an aspartic protease (i.e., it contains the amino acid aspartate in its active site).

The digestion of dietary proteins in humans begins in the stomach where the initial breakdown is normally done via the action of stomach secretions of pepsin and hydrochloric acid. The resulting amino acids and peptides make their way to the small intestine where further enzymes (e.g., trypsin) continue to digest the remaining peptides into amino acids and small peptides which can then be absorbed into the bloodstream. Some dietary proteins are more poorly digested than others and the presence of a significant amount of poorly digested dietary protein in the stomach can reduce the rate of emptying of the stomach leading to that overfull feeling.

The proteolytic action of pepsin in the stomach on dietary proteins may be assisted by consumption of plant-derived proteases such as actinidin.

### What is actinidin?

Actinidin is a unique cysteine protease from kiwifruit.



Actinidin tertiary (3D) structure, with secondary (2D) substructural domains such as  $\alpha$ -helices (coiled chains of amino acids) shown as coiled ribbons, and  $\beta$ -sheets (directional zig-zagging chains of amino acids) shown as arrows, adjoined by loops of intervening amino acid chains as one continuous folded polypeptide. From the Protein Databank (1AEC). Varughese KI, Su Y, Cromwell D, Hasnain S, Xuong NH (June 1992). "Crystal structure of an actinidin-E-64 complex". *Biochemistry* 31 (22): 5172–6.

The name actinidin is derived from *Actinidia*, which is the botanical (Latin) name for the genus of kiwifruit (e.g., green kiwifruit are *Actinidia deliciosa*). Actinidin was first proposed by Arcus in 1959 [1] after it was observed that raw kiwifruit prevents the setting of jelly,

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as the kiwifruit protease digests the jelly's gelatin. Actinidin can also be referred to as “*Actinidia* anionic protease”, “actinidain” and “Act d1”.

Actinidin constitutes up to 40% of the soluble protein in the green Hayward kiwifruit cultivar [2] which is the most prevalent commercial variety [3].

Compared to other fruit cysteine proteases, such as bromelain and papain, actinidin has the most acidic pH optimum, and a temperature optimum (40°C) closest to body temperature (37°C). This suggests it may be the most suitable plant protease for aiding gastric digestion of dietary protein.

### Effect of Actinidin on protein digestion

Actinidin has been the subject of a number of studies assessing its effect on the digestion of proteins both in the laboratory (*in vitro*, literally “in glass”) and in the body (*in vivo*, “in life”). Actinidin has a very broad specificity compared to pepsin and can hydrolyse a wide range of peptide bonds that are unavailable to pepsin. This action may then open up more target sites for pepsin activity. Research shows there is clear evidence that the consumption of green kiwifruit, kiwifruit-derived products like Actazin®, and the enzyme actinidin itself, can provide enhanced upper-tract digestion (particularly in the stomach) of a variety of dietary proteins, which lends support to a role for dietary actinidin as a digestive aid.

Actinidin extracts or actinidin found in whole kiwifruit powder like Actazin® have the ability to:

- enhance the digestion of proteins, including:
  - » dairy proteins – casein (major milk protein), yoghurt and cottage cheese [4]
  - » animal meat proteins (beef, chicken and fish) [4,5,6,7]
  - » plant proteins, including soy, rice, hemp, pea and wheat gluten [4,5,7,8,9]
- increase the rate at which the stomach empties [6,7]
  - » With faster stomach emptying, feelings of fullness, bloating, and stomach discomfort are reduced [10].

– increase the rate of amino acid absorption into the blood [11].

» This has been shown in a human study [11] where healthy older people consumed green kiwifruit containing actinidin with ground beef. The presence of actinidin in the stomach led to a more rapid increase in blood essential amino

acids (Fig. 1A), branched chain amino acids (Fig. 1B) and leucine (Fig. 1C) concentrations compared to the control (gold kiwifruit without actinidin).

» Faster absorption of amino acids can help to increase muscle mass and aid recovery of muscle after strenuous exercise.

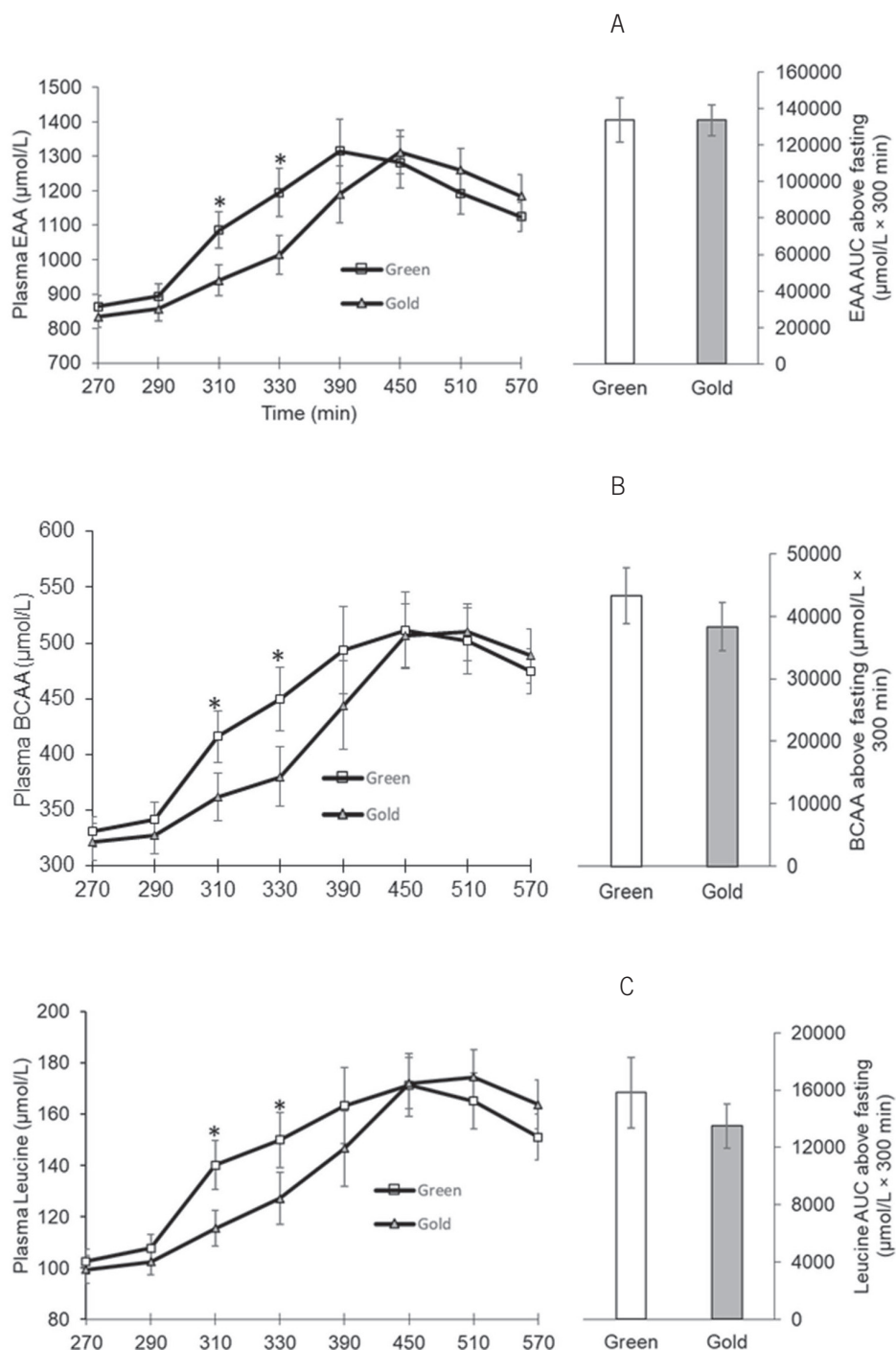


Fig. 1: Green kiwifruit consumption increases rate of plasma responses (concentrations in micromoles per litre of plasma) of A) total essential amino acids (EAA), B) branched chain amino acids (BCAA), and C) leucine following a meal of cooked beef and kiwifruit. There was a significant time by treatment interaction for EAA, BCAA and leucine ( $p < 0.01$ ). \*Statistically significant between the kiwifruit treatment ( $p < 0.05$ ). Values expressed as means  $\pm$  SE [11].



### Possible applications of actinidin

Given actinidin's ability to digest proteins it will be suitable for the following uses:

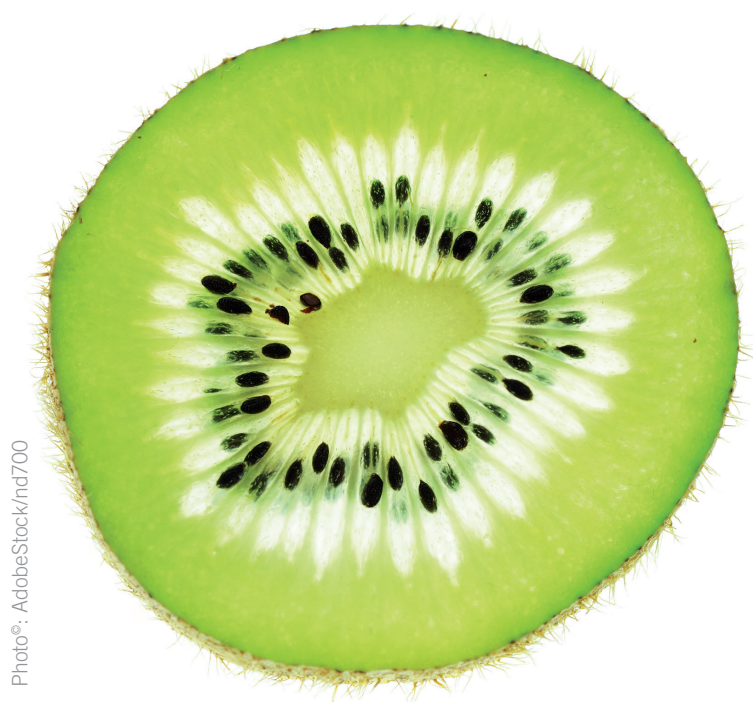
- Assisting digestion of dietary proteins (including protein powders) by,
  - » reducing feelings of fullness and discomfort; and
  - » releasing amino acids to be utilised by the body, for example in building/repairing muscle, creating enzymes and other important proteins.
- Meat tenderisation.

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Sri Lanka: Island of spices

## Ceylon cinnamon and pepper: aroma with added health benefits

Sri Lanka is famous for its spices. It is the home of cinnamon, pepper, cloves, cardamom, nutmeg and vanilla. But the tropical climate also supports cultivation of curry leaves, lemongrass, ginger, turmeric and many more products renowned for their good flavour. In addition, many spices are also valued for their health benefits or used as fragrances. Trade with cinnamon and pepper has a long tradition in Sri Lanka and today these products are still in demand on international markets: Ceylon cinnamon and Ceylon pepper are distinguished by their taste as well as their constituents and are vastly different from the products of the same name grown in other countries. The Import Promotion Desk (IPD), a project of the German Federal Ministry for Economic Cooperation and Development, has been involved in Sri Lanka since 2018, preparing small and medium-sized enterprises for the European market. Among them are many producers of organic cinnamon and pepper.

### Ceylon cinnamon vs. cassia cinnamon

Ceylon cinnamon is often referred to as the true cinnamon compared to cassia cinnamon. The spices differ in origin, production, coumarin content and flavour. Ceylon cinnamon is obtained in Sri Lanka from the bark of the cinnamon tree (*Cinnamomum zeylanicum*) native to the island. It contains high levels of antioxidants, secondary plant compounds and essential oils – but hardly any coumarin. Coumarin is found mainly in Chinese cinnamon, cassia cinnamon (*Cinnamomum cassia*), and can be harmful to health in larger quantities. For production, the bark is removed from the branches and the underlying inner bark shaved off



in layers. As it dries, the bark then rolls up on its own. For cassia cinnamon fairly thick bark is used, whereas for Ceylon cinnamon many thin layers of bark are added to form the cinnamon stick. The constituents and production methods influence the aroma. In terms of taste, the two types of cinnamon therefore differ significantly from each other. The higher quality Ceylon cinnamon has a more delicate and less pungent aroma than cassia cinnamon.

### Production of cinnamon sticks

Ceylon cinnamon sticks consist of several very finely cut pieces of inner bark from the cinnamon tree, pushed into each other. The peeling of the cinnamon branches is done by hand. In Sri Lanka, cinnamon production is often a family tradition and the craft-work skills are passed down from generation to generation. At the IPD company “Savour Route”, 90 percent of the team is made up of women. They are experts at processing the branches and finely planning the inner bark. Many of the female employees have been working in the cinnamon industry for many years and have refined their techniques over time. As specialists in Ceylon cinnamon production, they are well paid and many of them are breadwinners for their families. The finer the layers, the better the taste of Ceylon cinnamon. After cutting, several layers are placed over and inside each other, the fresh bark automatically rolls up from both sides and cinnamon sticks are formed. In cross-section, a Ceylon cinnamon stick with its many layers resembles a cigar. Ceylon cinnamon sticks are offered in different qualities – depending on the diameter of the sticks. The thinner the sticks and the finer the individual layers, the higher the quality. The highest quality grade “Alba” indicates sticks with a diameter of 6 mm.

### Ceylon cinnamon and health

Since ancient times, cinnamon has also been used medicinally. Its oil has a disinfectant effect and was therefore used to treat wounds as well as in meat preservation. In traditional Chinese medicine, cinnamon is used, among other things, for its antibacterial effect.



Photo: SDS Spices

Ceylon cinnamon in particular is reputed to have many health-promoting properties. It is said to have a beneficial effect on digestion and is used as a remedy to reduce blood sugar, and to fight colds and fever. In addition, IPD companies from Sri Lanka offer high-quality essential oils made from cinnamon leaves and cinnamon bark. These cinnamon oils are produced by steam distillation of the leaves or bark and their main components are eugenol and cinnamaldehyde. While eugenol predominates in cinnamon leaf oil, cinnamon bark oil has a high proportion of cinnamaldehyde. Both essential oils have a warming effect and anti-inflammatory properties.

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### Sri Lanka and the international spice market

Cinnamon was one of the first spices traded in the ancient world. Arab traders brought cinnamon from Sri Lanka to Europe via the spice route. Other spices such as pepper, nutmeg and cloves from Sri Lanka have also been in demand around the world for centuries. Today, Sri Lanka exports about 30,000 tons of various spices annually.

Spice production in Sri Lanka is in the hands of small farmers. More than 70 percent of the cultivated land is managed in small farms and home gardens. The IPD supports small and medium-sized enterprises that process the products of small farmers for export to the European market. For example, the company “Pasanka” from the IPD program cooperates with 60 small farmers.

### Trademark “Ceylon Spices”

Before Sri Lanka became independent and a republic in 1972, the island bore the name Ceylon. The name is still used for the famous tea and spices to indicate the special quality of the products. The “Ceylon Spices” trademark from the Sri Lanka Export Development Board (EDB), a partner of IPD in Sri Lanka, identifies cinnamon, pepper, cloves and other spices that are 100 percent grown, produced and packaged in Sri Lanka. This year, the European Union granted Ceylon cinnamon geographical indication (GI) status. This seal documents Ceylon cinnamon’s association with Sri Lanka and specifies that the raw material for Ceylon cinnamon must come from Sri Lanka.

### Ceylon pepper with high piperine content

Due to the proximity to the equator and the tropical climate, many different spices grow in Sri Lanka. The second most important raw material among spices, after Ceylon cinnamon, is Ceylon pepper. It differs from other pepper varieties and countries of origin in its high piperine content (7 to 15 percent). Its particular pungency makes it exceptional. The flavour of Sri Lankan black pepper is richly aromatic, with floral and citrus notes, while maintaining a strong pungency. The flavour only really comes through when the grains are freshly ground. Pre-ground pepper quickly loses its volatile oils and thus its flavour characteristics.

### Ceylon pepper production

Ceylon pepper comes from the pepper bush (*Piper nigrum*), which is grown on an area of 32,800 hectares in Sri Lanka. Depending on the time of harvest and further processing, there are different types of pepper, such as green, red, white and black. For the classic black pepper, the berries of the *Piper nigrum* are harvested when they are green and not yet fully ripe. Then they are blanched and dried



Photo®: SDS Spices

in the sun, producing peppercorns with a high essential oil content. The black colour results from the oxidation that takes place during drying.

### Ceylon pepper and health

Black pepper – similar to cinnamon – is also used as a remedy in traditional medicine due to its warming effect. In Ayurveda as well as in traditional Chinese medicine, the warming spice is used for colds and digestive complaints. An essential oil is also extracted from the black peppercorns. Sri Lankan companies use steam or hydro distillation for this. Pepper oil is considered a good remedy for colds due to its antiviral and antibacterial effect, and it is also said to promote circulation.

### High-quality spices in organic quality

In Sri Lanka, the development of organic agriculture is of great importance. One of the country’s goals is to convert the industry to 100 percent organic. Already today, the well-known Ceylon spices are mostly offered in organic quality – a special feature on the spice market. The companies “Verger Naturals” and “SDS Spices”, which the IPD has been accompanying since 2019, offer their entire range of spices with international organic certifications – including cinnamon, black and white pepper, cloves, nutmeg and mace.

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## The power of natural astaxanthin: Inner and outer cell protection with AstaFit® and AstaCos®

Monika Siebel PhD., Katharina Müller

Our skin, the largest body organ, plays an important role in our lives. Its health and morphology determine our outer appearance and essentially contributes to our own wellbeing. As a protective shield, the skin is constantly exposed to outer environmental influences and stress which is caused by internal factors like physical exertion and external factors like UV rays.

The skin's systemic supply with micronutrients, e.g., by nutriment or specific supplementation, is by far the most important parameter contributing to healthy skin. This fact becomes especially visible in the way deficiency states influence the skin.

By combining topical applications and oral intake of an active agent, the effectivity of the use and the results are enhanced. Eventually, a holistic application yields the best possible result. To preserve and support our skin functions, numerous agents can be

used internally and externally; however, not all entail this combined efficacy. An encompassing membrane permeability is as essential as lipophile and hydrophilic structures which enable an accumulation within the various membrane layers. Antioxidants form an important group as they are able to neutralise stress factors in the skin.

Algae-based astaxanthin is not only considered as strongest natural antioxidant but meets the above-mentioned requirements for a perceptible topical and oral intake. It belongs to the group of carotenoids, especially xanthophylls, and it is specifically effective thanks to its unique molecular structure (carbon, hydrogen and oxygen atoms). (1) In the microalga, the molecule astaxanthin is directly tied to phospholipids and exists as monoester or diester, depending on whether the fatty acids react with one hydroxyl group or with both hydroxyl groups. Hence, the excellent membrane mobility of algae-based astaxanthin is maintained and the higher bioavailability is substantiated compared to other natural astaxanthin sources like bacteria or yeasts. (2) As an active agent, astaxanthin is gently gained from the *Haematococcus pluvialis* biomass by extracting CO<sub>2</sub>; furthermore, it is water-soluble. For dietetic purposes, it can directly be used as natural oleoresin (AstaFit®) and combined with other vital substances. As cosmetic ingredient, it is further refined/purified with jojoba oil.

Due to its fat-soluble characteristics, astaxanthin-rich oleoresin offers numerous ways of processing and can be further micro-encapsulated by refining processes through which areas of application can again be exponentiated.

### Light-induced oxidative stress & the role of ROS (reactive oxygen species)

Especially during the neutralisation of free radicals, so-called “reactive oxygen species” (ROS), antioxidants play a major role. Astaxanthin is considered as “diamond among scavengers”, while its significance regarding the reduction of oxidative stress is largely scientifically documented. (1)

Light-induced oxidative is a key issue regarding the human skin-ageing and causes skin damage. Whenever skin molecules absorb UV or visible light and transfer energy to oxygen, they transition into an excited state and form singlet oxygen – an extraordinarily reactive molecule whose influence on the cellular DNA is especially catastrophic for the skin. Skin photosensitisers are endogen and exogen compounds that are activated easily by UV or visible light and, as soon as this sensibilisation has occurred, trigger adverse skin reaction. Hence, they transfer the charge onto oxygen and produce ROS as well as free radicals. The light-induced ROS and free radicals lead to oxidative stress, devastate proteins, lipides and DNA and cause negative changes of the skin structure.

When singlet oxygen attacks the cell membranes, it activates enzymes that lead to cellular death, peroxidation and, finally, to an amelioration of the skin texture. A singlet oxygen molecule can insert a single 8-OH-dG (8-hydroxydesoxyguanosine – biomarker for oxidative stress) into a DNA molecule. This process prompts the so-called NF- $\kappa$ B cascade (nuclear factor “kappa-light-chain-enhancer” of activated B-cells) – that’s the beginning of an inflammation entailing a chain reaction of thousands of molecular modifications within the cell, membrane as well as the over-expression of MMP-1-enzymes destroying collagen and other elastic fibres. In further consequence, skin damage and skin-ageing are further advanced. (1), (3)

### Light-induced oxidative stress & possibly triggering factors

Light-induced oxidative stress is triggered by various forms of radiation, e.g.

- UVA radiation
- UVB radiation
- Blue light

UVA and UVB radiation (ultraviolet light) and infrared light are accountable for about 50 to 80 % of visual skin-ageing. Hence, light protection from the outside through cosmetical approaches and from the inside through targeted nutritional supplement is a possibility to protect the skin from damage. Especially the amount of UVB rays in sunlight is

a decisive, well-characterised factor for skin damage. UVB radiation, a high-energy, short-wave radiation (290 to 320 nm), generally stresses the epidermal part of the skin.

By contrast, the UVA proportion in sunlight is lower in energy and of long-wave nature (320 to 400 nm). This kind of irradiation can enter the dermal parts of the skin, which may lead to long-term damage of the collagen and elastin fibres. The human skin possesses intrinsic cellular protection measures that can regulate the amount of ROS induced from the outside down to a tolerable level. This natural mechanism can be overstrained by regular and continuous UV irradiation, and it declines over time. (4)

Exactly like UVA and UVB radiation, blue light also has essential effects on the skin as it induces oxidative stress, especially in mitochondria. By using a UV-Vis spectroscopy in a study in 2021, it was determined that astaxanthin’s maximum absorption effect amounts to 476 nm. A wavelength of 400 to 480 nm is referred to as blue light. Hence, the assumption is suggested that astaxanthin is able to protect against blue light as well (Fig. 1). (5)

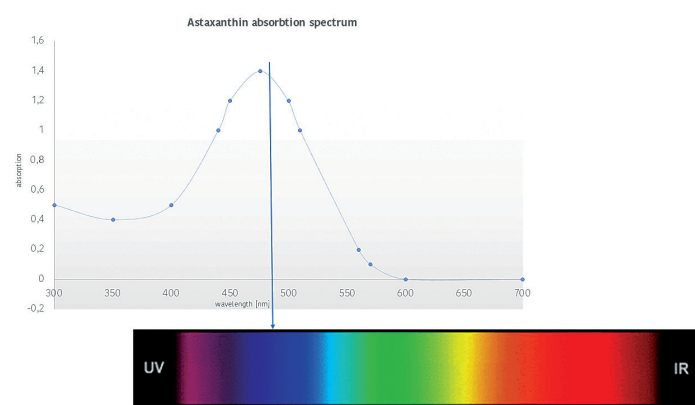


Fig. 1: UV-Vis astaxanthin spectrum

Astaxanthin (AstaFit® and AstaCos®) is essential to lessen premature photo-ageing and it is an ideal supplement to SPF filters. (6)

Studies have proven that oral supplementation with natural astaxanthin protects all skin layers, thus promoting healthy, glowing skin from the inside. A study from 2017 suggests that continuous astaxanthin intake reduces



oxidative stress and, subsequently, leads to morphological alterations of the further skin surface elements (RSSCs), which is consistent with a reversion of the skin-ageing process. The study lasted 4 weeks and comprised 31 participants (17 male, 14 female) above 40 years of age who obtained a daily dose of 4 mg of astaxanthin. (7)

Also, the effect of nutritional supplement with astaxanthin on skin damage induced by UV radiation was investigated in 2018. To assess astaxanthin's protective factor for skin damaged by UV rays, researchers determined the minimum erythema dose (MED) and analysed the UV radiation-induced alterations of the moisture content and the transepidermal loss of water (TEWL) of 23 test persons who were supplemented with 4 mg of astaxanthin per day – both at the start of the study as well as after 9 weeks of supplementation.

The study's result indicates a rise of MED (Fig. 2) inferring higher security regarding UV radiation, moisture reduction in the irradiated areas (Fig. 3) and an enhancement of coarse skin as well as of the skin texture in the astaxanthin group. (8)

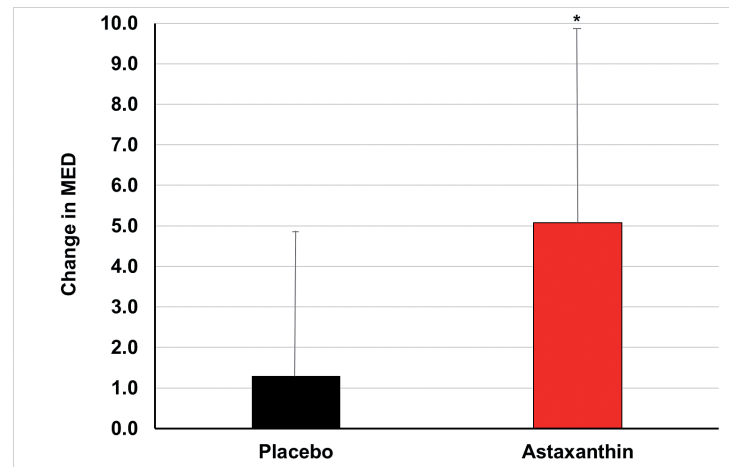
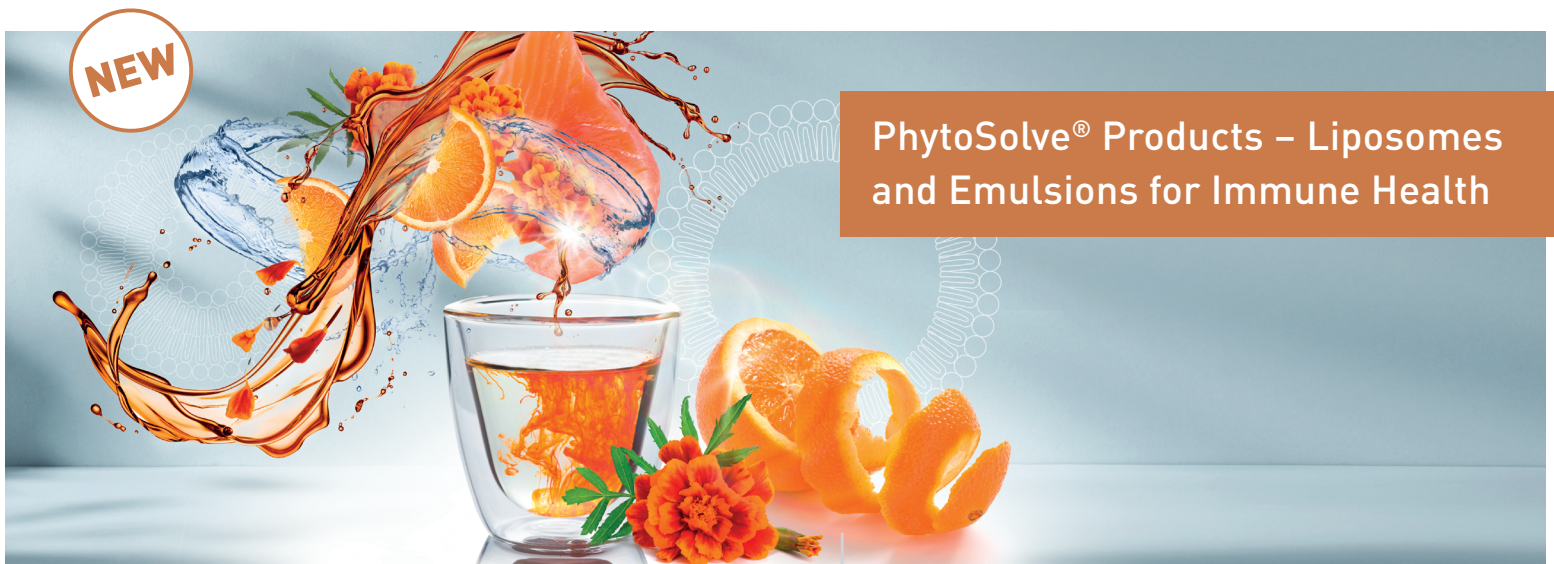


Fig. 2: Alteration of the minimum erythema dose (MED) compared to the initial value in both groups. The error bars show the standard deviation.

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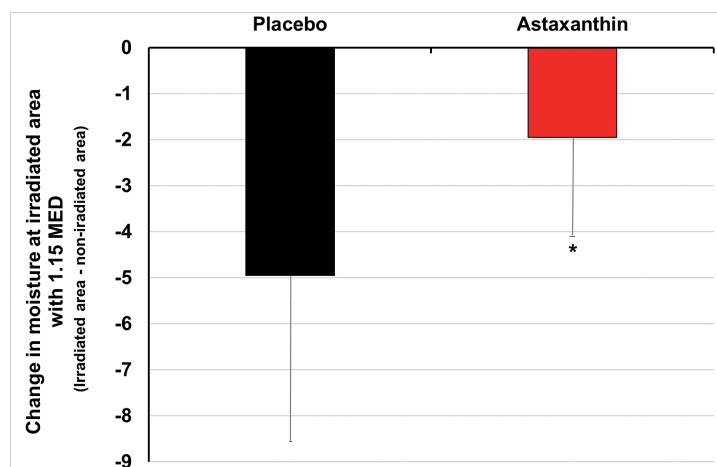


Fig. 3: Nutritional supplement with astaxanthin lessens the moisture reduction in the irradiated areas. Alteration of moisture 7 days after irradiation. The error bars indicate the standard deviation.

In a current dermatologic in-vivo study from 2021 with topical application of astaxanthin, the protective effect of the astaxanthin oleoresin AstaCos® against the impact of UV radiation was confirmed. In a clinic pilot study, the agent was used with a concentration of 0.2 %. Its UV protection, compared to a placebo, was tested in a controlled experimental design with 21 healthy test persons of Fitzpatrick skin type 2 or 3 (Fig. 1). After intensive UV exposure, an erythema value lower by 25% compared to the placebo group was measured with the AstaCos® treatment (Fig. 4). In this experimental design, the agent suppresses the visible formation of erythema in over 70% of cases. (9)

In another in-vitro study in 2021, keratinocytes being exposed more intensively to UVB irradiation were compared. The cells treated with AstaCos® proved biological cell protection as opposed to UVB irradiation, while less cell damage was noticeable histologically. (6) Astaxanthin's effect compared to UVA-induced oxidative stress was also confirmed in an in-vitro study with human fibroblasts. Compared to other antioxidants, including beta-carotene and canthaxanthin, astaxanthin is more powerful. The results support the conclusion that astaxanthin offers significantly higher light protection, as opposed to beta-carotene and canthaxanthin, and counteracts above-mentioned UVA-induced damage. (10)

### Combining the best of two worlds

The described research documents an optimum result for the skin by oral or dermal intake of astaxanthin. Astaxanthin also has an effect as biological cell protection against the effects of harmful UVA and UVB rays and can reduce wrinkles, boost the skin's elasticity and prevent skin-ageing. The agent guarantees an encompassing reduction of



Fig. 4: Left – measuring with Skintrek PT3 exposure item. Right – photo documentation of an in-vivo study to measure the protective effect of AstaCos® against the impact of UV radiation. Right and left lower arm after 24 hours of identical UV irradiation on both sides (right lower arm: placebo, left lower arm: topical astaxanthin): left lower arm without erythema, right lower arm with erythema in the exposed test areas.



oxidative skin stress – it functions right there where it is needed, thus getting into deep skin layers. Through this inner and outer protection, our skin is optimally prepared to protect us, as a barrier, against daily harmful environmental influences.

#### About BDI-BioLife Science

BDI-BioLife Science specialises in the development of technologies to produce high-quality algae valuable materials for the life sciences industry. With a specifically developed closed algae-breeding method at the cultivation plant at Ökopark Hartberg, Austria, BDI-BioLife Science manufactures premium-quality natural astaxanthin tailor-made for the cosmetics (AstaCos®) and nutritional supplement (AstaFit®) industries.

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## Live well for longer

Collagen peptides stimulate the body's own collagen production, thus supporting mobility and better quality of life

Martin Walter

Our body is truly miraculous, with numerous processes occurring silently and simultaneously in order for it to maintain optimal function. For example, even as you're reading this, your body is busy breaking down and rebuilding proteins. These include the structural protein collagen, which keeps the body in shape, ensures the function of the musculoskeletal system and performs important tasks in many other parts of the body, such as the eye, blood vessels and intestinal wall. In a young, healthy body, up to 400 g of protein are replaced by new protein mass every day. In this way, the body renews itself continuously and ensures that we remain healthy, active and mobile for as long as possible into later life. However, metabolic processes slow down with age, and the breakdown of proteins begins to outpace their regeneration. Although this process cannot be stopped, it can be slowed through supplementation with certain nutrients. Collagen peptides are

a prime example, as they help stimulate the body's own collagen production – and thus improve quality of life even in old age.

### All about ageing

It's important to understand that getting older is really not such a bad thing. And while it's obviously unrealistic to assume that seniors will be able to function as well in retirement as they did in their mid-20s, for example, the ageing process is forever changing and evolving. This is largely as a result of a dramatic increase in life expect-



tancy over the past 150 years. While men and women were predicted to live for approximately 40 years in the 1900s, the German Federal Statistical Office says the average life expectancy is currently 83.4 years for new-born girls and 78.6 years for new-born boys, based on the results of the 2018/2020 mortality table.

So today, it's less about getting old and more about maintaining good health for as long as possible. One of the great fears of older people is losing their independence as a result of a declining musculoskeletal system – whether due to sarcopenia, advanced osteoporosis or degenerative joint diseases. It's clear, then, that the ability to remain mobile and active into old age really does have a huge impact on quality of life. That's why so many people are keen to take a preventive approach to wellbeing, be it through sport, a balanced diet or both.

### Impact of decline in body's most abundant protein

The fact is, the human body is programmed to be finite. With age, processes in the body change, the metabolism slows down and the ability to absorb and process nutrients decreases. Tissue production also changes, as does collagen production, which begins to decline after the age of 30. As a result, our skin tells us in no uncertain terms that our bodies are beginning to age. The skin stores less moisture, collagen content decreases and wrinkles become visible. Collagen not only plays an important role in the skin, however, but also many other parts of the body.

With a share of just under 30 per cent, it is the most abundant protein in humans and the most important building block of connective tissue. As a structural protein, it performs important functions in joints, bones, tendons and ligaments, as well as in muscle tissue and fasciae that run through the entire body. The entire musculoskeletal system is held together by collagen-containing structures that, among other things, convert muscle power into movement. In short, when an ageing body produces less collagen, mobility can suffer. Cartilage tissue in the joints diminishes, bones lose stability, and tendons and ligaments lose flexibility and resistance.

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### How do collagen peptides work?

The good news is that it's possible to counteract the decline in the body's production of this essential protein through supplementation with collagen peptides. These are highly purified, short-chain protein building blocks of animal origin that are obtained by partial hydrolysis of native collagen protein. As relatively small molecules, they have a molecular weight of less than 10,000 g/mol and consist of at least two – but up to as many as 100 – amino acids.

But how exactly do collagen peptides work? When our body breaks down collagen, these long chains of amino acids are broken down into small fragments by enzymes and transported away. As part of this process, the body receives a signal that pieces of degraded collagen are present and reconstruction must therefore begin. A young and healthy body reacts immediately, and does just that. However, when the metabolism slows down over time, these signals are no longer sufficient and degradation increasingly prevails.

When we consume collagen peptides through food, we absorb collagen fragments but in larger quantities. These fragments enter the bloodstream, distribute themselves throughout the body and the same process begins again: the cells responsible for connective tissue and collagen metabolism notice that there is an imbalance, and then send a much stronger signal to produce more collagen. As a result, the body's own mechanism is externally stimulated and simultaneously intensified, leading to increased collagen production.

### Specific peptides for particular needs

Current findings show that collagen peptides differ significantly from one another in terms of efficacy. Common to all variants are their rapid absorption and good bioavailability. However, not all collagen

#### A closer look at collagen's structure

To understand why collagen is so strong and flexible, it's important to look at its molecular structure. Natural collagen consists of chains of about 1000 amino acids each. Three chains of these amino acids spiral around each other to form a stable and mobile structure known as a triple helix. This is about 300 nanometres long and has a diameter of about 1.5 nanometres – about 100,000 times thinner than a human hair. Nevertheless, the special combination of amino acids ensures a very tight winding of the helix and a particularly densely packed structure. This is what makes collagen so stable.

peptides are also bioactive, i.e. have a direct effect on the body's own processes.

GELITA offers a range of specific Bioactive Collagen Peptides (BCP®) that stimulate collagen metabolism. These collagen peptides achieve an optimal effect when they reach the appropriate tissue cells. In total, there are four different groups of highly specialized tissue cells in the human body: Fibroblasts in the skin, tendocytes in the ligaments and tendons, chondrocytes in the joints and osteoblasts in the bone. To confirm the effect of the peptides, GELITA regularly initiates clinical studies, which are carried out at renowned, independent institutes. It has been shown that these cells react very specifically to certain peptides. This process can be roughly compared to the lock-and-key principle: The structure of the peptide fits exactly to the receptors of the respective tissue cell, which is then stimulated to produce collagen.

### Comprehensive peptide portfolio

GELITA offers a broad portfolio of Bioactive Collagen Peptides that reach all collagen-rich areas of the body. For example, VERISOL® helps improve skin texture; FORTIGEL® promotes the regeneration of articular cartilage, and FORTIBONE® contributes to bone density and stability by promoting the biosyn-





thesis of the extracellular bone matrix. With BODYBALANCE®, athletes can optimize their body composition through muscle gain and fat loss. TENDOFORTE® strengthens tendons and ligaments, and can thus contribute to both increased performance and a reduced risk of injury, with a faster return to training after injury. Furthermore, all the modes of action of GELITA's collagen peptides have been extensively and scientifically proven.

### Importance of maintaining good health

The possible positioning of collagen-containing products is as varied as the peptides themselves. Older people are without question an important target group, because as soon as the first aches and pains or real limitations in mobility become noticeable, the motivation to do something about them increases. But healthy ageing must start at a young age. Those who act preventively will be rewarded in later life. And consumers' willingness to take good care of themselves is on the rise. Figures from the market research company FMCG Gurus from 2021 show that more than half of people see maintaining good health as a long-term project. Yet just two years earlier, only 42 per cent of those surveyed responded that way. At the same time, people are now investing more in health education (2021: 58% vs. 2019: 39%) and showing greater interest in food ingredients that have proven health benefits (2021: 42% vs. 2019: 26%).

Physically active people in particular want to keep their own bodies strong and resilient. With their specific modes of action, collagen peptides can also offer real added value to this target group – be it to optimize body composition, accelerate regeneration or minimize the risk of injury to tendons and ligaments. For many women, collagen has been closely associated with beauty for years. Collagen peptides are suitable for beauty-from-within concepts that can improve the skin's appearance from the inside out, but also strengthen hair and nails.

For manufacturers, collagen peptides offer numerous possibilities because they are easy to process and are therefore suitable for a wide variety of product concepts – from tablets, capsule preparations and instant products, to bars and gels, drinks and shots. They have no negative impact on the taste or odour of the end product and are easily soluble, as well as heat- and acid-stable. In addition, collagen peptides are safe and, as natural foods, do not carry an E-number. They are therefore also suitable for clean label products.

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<sup>1</sup>Source: [https://www.destatis.de/DE/Presse/Pressemitteilungen/2021/07/PD21\\_331\\_12621.html](https://www.destatis.de/DE/Presse/Pressemitteilungen/2021/07/PD21_331_12621.html)

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## Cognitive health and stress reduction

3 questions for Ingredia regarding their milk protein hydrolysate

### What specific ingredients related to cognitive health or stress reduction do you offer brands in supplement applications?

Ingredia's dairy-based bioactive ingredients are used in numerous applications such as dietary supplements or functional foods and beverages. They are clinically proven and sought after for their recognized positive effects on health and well-being.

Ingredia has developed Lactium®, a milk protein hydrolysate which contains a bioactive decapeptide with soothing properties. This peptide, also called  $\alpha$ -casozepine, is produced from the milk protein thanks to a "food grade" tryptic hydrolysis. Lactium® decreases anxiety-related symptoms and helps consumers better manage their emotional state, whether it is induced by occasional or everyday anxiety.

Long before it reached the market, Lactium® was the subject of numerous assessments on toxicity or side effect according to OECD

(Organization for Economic Cooperation and Development) guidelines and Good Laboratory Practices. These demonstrated that Lactium® presents no health risks at the recommended doses: no undesirable side-effects, no acute or chronic toxicity, no memory loss, no habituation, no addiction, no sedation, no disinhibition.

### Are there new advancements and studies available to enhance new product innovations?

8 consumers in 10 are satisfied with Lactium® after our 9 clinical studies performed on more than 500 persons. In 2021, we wanted to address a core objective for all our customers: consumer satisfaction. We recruited 300 persons in the world, in 3 distinct regions – namely USA, France and China. We applied a strict methodology with validated questionnaires and partnered up with BioMerieux for their well-known expertise in the area. 300 persons took Lactium® at 300 mg/day during 30

days, with either the indication stress or sleep disturbance indication.

The results showed an overall 78 % satisfaction, quite evenly splitted in: 78% in the stress indication and 77 % in the sleep disturbance indication.

### Are there specific DSHEA compliant product label claims for your ingredient(s)?

Ingredia: In April 2020, US FDA authorized 7 claims for Lactium®. The dietary supplements manufacturers featuring Lactium® in their products for adults will be able to communicate on the benefits of this unique bioactive. As a natural ingredient, Lactium® can safely be used by the whole family.

For more information, please visit

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## Chicory champion for immune and digestive health

Prebiotic fibres from chicory root promote growth of good gut bacteria for improved wellbeing

Anke Sentko

Maintaining a healthy immune system has become more important than ever in the wake of COVID-19, and the subsequent pandemic. With the ever-growing awareness of the proven link between a strong immune system and the gut's microbiome, a great deal of attention is now being paid to the important role played by nutrition in the modulation of the body's defence and digestive mechanisms. Here, prebiotic fibres from chicory root inulin and oligofructose are ingredients that have been scientifically proven to have a beneficial effect on the gut's microbiota composition, as well as digestive health and overall wellbeing.(1)

### Gateway to the human body

Every day, the body's largest digestive organ – the intestinal tract – comes into direct contact with not only food and drink, but also a large variety of different microorganisms and their metabolites, breaking down products and other substances. It is respon-

sible for the digestion and absorption of nutrients, and their subsequent transportation into the blood, as well as preventing potential pathogens – such as harmful bacteria or viruses – from disrupting normal bodily functions.

Here, the so-called intestinal barrier, a thick layer of mucus formed by intestinal mucosal cells containing different antigens as well as defence cells of the immune system, plays a key role. The efficiency of the intestinal barrier is closely linked to the gut microbiome – a collection of bacteria that reside in the gut. In fact, the gut hosts one of the most complex ecosystems on the planet, as it's home to more than 100 trillion microorganisms. The composition of these microbial cells is highly complex, particularly when it comes to a balanced ratio of beneficial, neutral, harmful and potentially harmful bacteria.

### Targeted support for the intestinal microbiome

The human microbiome combines different types of microorganisms. Some of them, such as lactobacilli or bifidobacteria, are classified as “good” bacteria. Other bacteria, for example, escherichia coli, are known as “bad” bacteria as they are potentially harmful, particularly when present in excessive amounts. In a healthy body, beneficial, neutral, potentially pathogenic and pathogenic microbiota coexist in a balanced relationship so that the bad bacteria do not “take over”.

But if the equilibrium of the intestinal ecosystem is disrupted, i.e. by infectious illnesses, the prolonged use of antibiotics or old age, imbalances – so called dysbiosis – might occur, which is associated with weaker health and growing susceptibility to a number of diseases.

Therefore, maintaining a balanced composition within the intestinal microorganisms and supporting beneficial bacteria is seen as one of the key factors in the maintenance of digestive health, as well as strong resistance to infections. In fact, our intestine comprises the largest part of our immune system, as around 70% of immune cells are present in the gut. Here, the role of daily nutrition cannot be overestimated, as it has a direct impact on both digestive and inner defence systems.

The gut microbiota lives on food residues that bypass absorption in the small intestine, and serve as feed for the intestinal microorganisms living in the large bowel. While proteins favour the microorganisms that are involved in proteolytic fermentation, which is known to lead to a number of potentially toxic and harmful metabolites, prebiotic dietary fibres trigger saccharolytic fermentation. Saccharolytic fermentation significantly stimulates the production of short chain fatty acids and reduces the pH in the colon. A lower pH limits the growth of some harmful bacteria that favour an acidic environment. This, in turn, positively influences the gut environment and improves the outcome for overall health and wellbeing.

Chicory root fibres are the preferred feed for bifidobacteria as bifidobacteria have the enzyme to split the  $\beta(2-1)$  linkage within the individual units of which inulin is comprised. Therefore, bifidobacteria have a competitive advantage when feed that contains inulin is offered to them, as they are better nourished and grow faster than others. As non-digestible food components, dietary fibres reach the colon almost intact. Some are excreted as such via the faeces, as the gut microbiota cannot break them down. Other food residues are fermented in a general way, while certain other dietary fibres, e.g. inulin and its shorter chain fructans component also called oligofruc-

tose or fructooligosaccharide, are selectively fermented by a specific part of the gut microbiota, the bifidobacteria, with short chain fatty acids the primary end products of this fermentation process. Prebiotic dietary fibres promote the faster growth of good bacteria and increase their overall presence. Experts in the field describe a prebiotic as “a substrate that is selectively utilized by host microorganisms conferring a health benefit”.(2)

Additionally, the formed short-chain fatty acids serve as energy suppliers for the intestinal cells, alongside other metabolic products that support internal defence mechanisms and have a positive effect on digestion. Among other things, they promote the protective function of the intestinal barrier and thus also reduce the risk of so-called leaky gut syndrome – an increased permeability of the intestinal wall.

### Prebiotics from chicory root

According to the International Scientific Association for Probiotics and Prebiotics (ISAPP), there are just a few fibres that are scientifically proven prebiotics. These are galactooligosaccharides (GOS) as well as prebiotic fibres derived from chicory root – inulin and oligofructose (short-chain inulin).

With Orafit® Inulin and Oligofructose, BENEØ offers dietary prebiotic fibres extracted via gentle hot water extraction from the chicory root – a particularly rich source of inulin. Oligofructose is then derived from inulin through partial enzymatic hydrolysis, a process that occurs naturally in the chicory root during the late harvest period. Thus, the prebiotics from BENEØ are 100% of vegetable origin.

Besides their positive effect on the growth of beneficial bacteria, these natural prebiotics have also been proven to promote higher stool frequency and an overall healthier digestive system.(3) On 12 December 2015, the European Commission has authorised a 13.5 health claim for BENEØ chicory root fibre inulin and the support of digestive health. This allows information related to Orafit® Inulin and its promotion of digestive health to be conveyed to the consumer, based on scientific research that proves it increases stool frequency thanks to its positive effect on bowel function.(4)

Additionally, The Chinese Nutrition Society (CNS), China's largest professional nutrition body, has concluded that inulin and oligofructose are among the first accepted prebiotics. This recognition includes BENEØ's functional fibres derived from chicory root and is a result of the premier prebiotic scientific consensus statement in China announced in 2021. The statement defines prebiotics and its criteria for ingredient classification.(5)

### Improved digestive wellness – backed by science

There are currently more than 50 human intervention studies that have addressed the selective growth of bifidobacteria through the consumption of prebiotic dietary fibres from chicory root. One such



Photo®: BENEØ



study, conducted in 2017, focused on the impact of chicory root fibre fermentation and assessed its consequences both on the composition of the colon bacterial ecosystem, and faecal metabolite profiles. Looking at the whole gut microbe ecosystem, the analyses detected specific inulin-induced changes in relative abundances of three genera – increase in the good bacteria bifidobacteria and anaerostipes, and decrease in the potential pathogen bilophila.(6)

The researchers used a state-of-the-art technology called “next generation sequencing”. While the selective increase in bifidobacteria due to inulin and oligofructose has been previously demonstrated in different intervention studies, selective fermentation could be confirmed by the use of this technology. The researchers found a direct link between the consumption of chicory root fibres, decrease in bilophila, and improvement in quality of life in the subjects who were mildly constipated. Lower bilophila numbers were associated with softer stools, reduced discomfort and improved quality of life. This study is further proof of the role that gut microbiota plays in overall wellbeing, opening the field for exciting research in this area.

### Immune support – even for children

Just like adults, babies and children also need a strong immune system. For babies and small children, the support of digestive health and the immune system is even more important as the gut and the immune system is still developing. A large-scale, randomized controlled trial involving more than 200 kindergarten pupils in Hungary was able to demonstrate improved digestive health and strengthened defences in children, thanks to chicory root fibres.(7)

The study, which focused on children aged 3–6, examined the effect of supplementation with a daily dosage of 6 g of chicory root fibre during the autumn and winter. Conducted over 24 weeks in total, with a double-blind, placebo-controlled design, the study demonstrated various health benefits among children, including fewer incidences of infections and episodes of fever requiring a physi-

cian consultation. It highlighted that the risk of infections can be reduced by incorporating chicory root fibre, Orafit® inulin, into the daily diet of children to strengthen their body's defences. The research also confirmed that chicory root fibre was very well tolerated, and supported the children's gut microbiota by increasing bifidobacteria and lactobacilli numbers. In addition, the positive effect on digestive health was further supported by a softer stool consistency. The researchers were also able to prove

that prebiotic chicory root fibre supports the gut microbiota balance in children even after antibiotic treatment.(8) Antibiotics are known to significantly damage the microbiota, creating a microbial imbalance in the gut which may affect health in later years. The findings showed that regular consumption of prebiotic chicory root fibre reduces the antibiotic-induced disturbances of the microbiota composition. In general, the children undergoing antibiotic treatment showed a reduction of microbiota, including benefi-

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cial gut microorganisms. However, those children also receiving the prebiotic supplementation demonstrated a significantly higher presence of bifidobacteria versus the control group.

In breastfed infants, bifidobacteria make up the majority of their intestinal environment. Breast milk contains prebiotics by nature, thus stimulating the growth of beneficial microbiota in a child's gut. This promotes maturity of the digestive and immune system – neither of which is fully developed at birth. Inulin and oligofructose support the increase of bifidobacteria in the intestines of infants and young children. A meta-analysis reviewed the effectiveness of prebiotics in preventing acute infectious diseases in children 0–24 months of age.<sup>(9)</sup> This showed a statistically significant decrease in infections requiring antibiotic treatment in the prebiotic groups compared with the placebo groups. The researchers further concluded that in this age group, "the available studies show that prebiotics may also reduce the overall number of infections".

### Prebiotics: Healthy from nature

Inulin and oligofructose are of interest to the food industry for several reasons: Products enriched with prebiotic dietary fibres meet consumer desire for foods supporting a healthy and preventive diet. That is because many consumers now see a direct link between digestive health and a strong immune system, as revealed in analysis by market research company Health Focus International in 2020:

Three-quarters of respondents believed that positive effects of a healthy gut included "general physical health" and two-thirds cited a "functioning immune system". Orafit® Inulin and Oligofructose allow food manufacturers to better cater for the growing market interest in foods enriched with prebiotic fibres, and suitable for numerous applications in different food segments: dairy products, cereals, baked goods, beverages, confectionery and fruit preparations, as well as baby food and infant milk.

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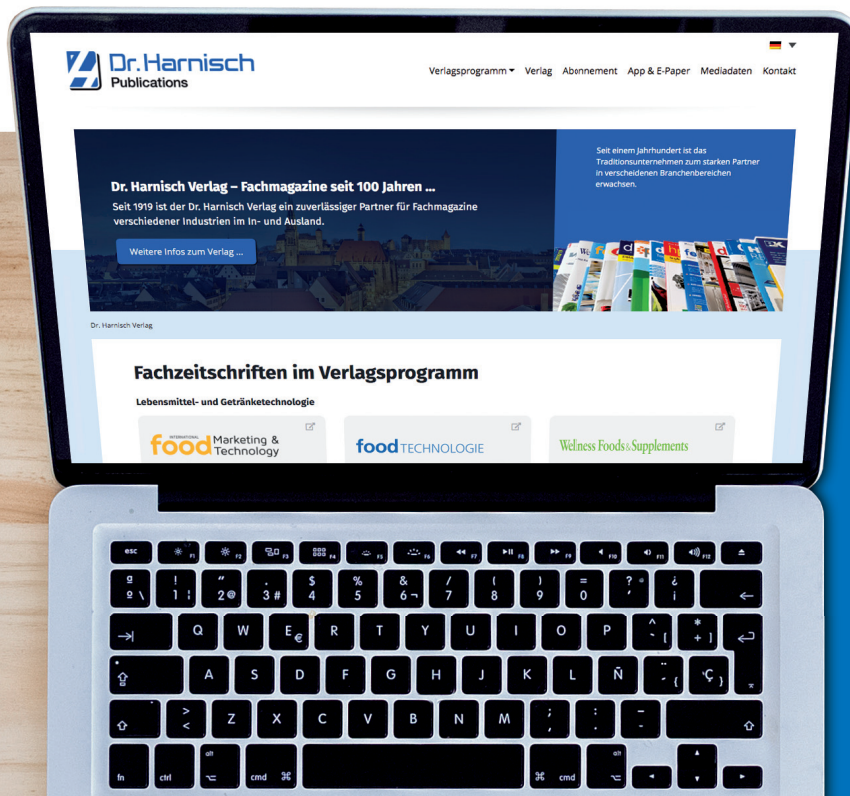
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