

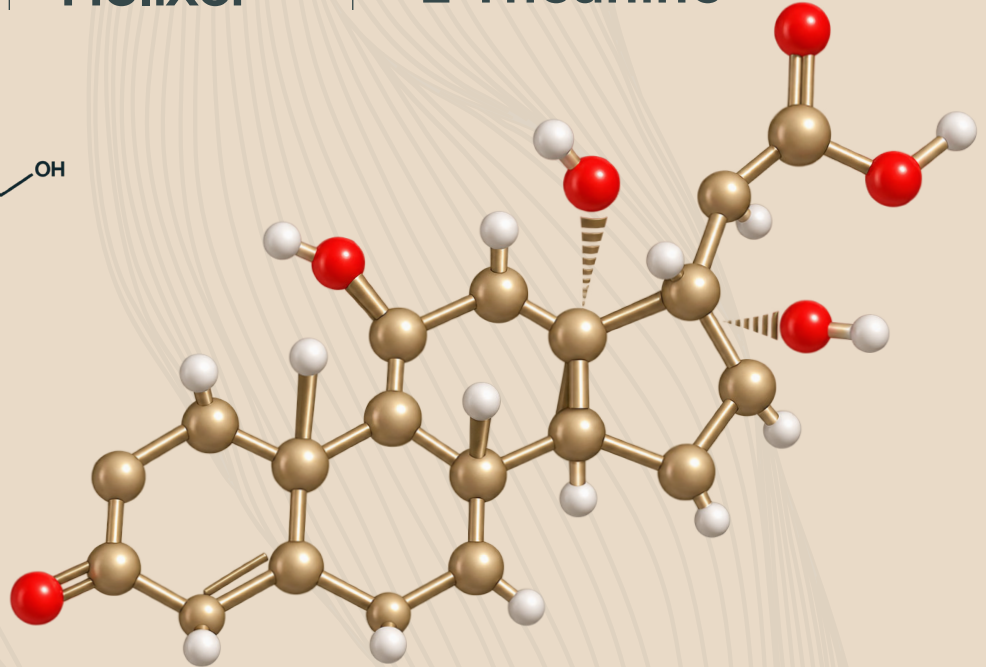
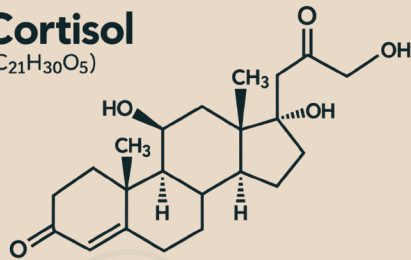
CORTISEN[®]

Lactium[®]

Holixer[™]

L-Theanine

Cortisol
(C₂₁H₃₀O₅)



Stress is not just a feeling.
It is a measurable physiological response.

For healthcare professionals only

Clinically studied¹
nearly **3 times lower**
cortisol concentration*

* in newly grown hair



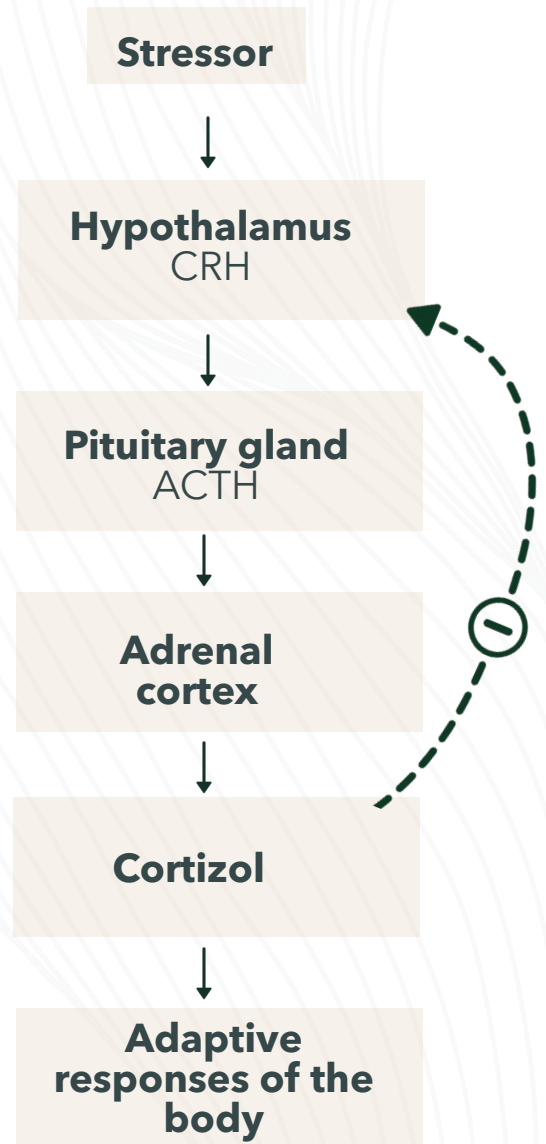
HOW DOES THE CORTISOL RESPONSE WORK?

When a stressor is detected, the HPA axis - the hypothalamic-pituitary-adrenal axis - is activated, representing one of the central neuroendocrine stress response systems.

The hypothalamus releases **CRH** (corticotropin-releasing hormone), which stimulates the secretion of **ACTH** (adrenocorticotrophic hormone) from the **pituitary gland**. ACTH then acts on the adrenal cortex, triggering the release of **cortisol**. Cortisol enables the body to adapt to increased physiological and metabolic demands, including by providing more readily available energy sources.

As cortisol levels rise, cortisol exerts negative feedback, inhibiting the release of CRH in the hypothalamus and ACTH in the pituitary gland, thereby limiting further activation of the HPA axis. This mechanism is important because it prevents excessive or prolonged activation of the HPA axis and helps regulate the stress response. Once the stressor has passed, the activity of the system gradually decreases and the body returns towards its baseline state.

With prolonged or repeated stress, regulation of the HPA axis may change, which may also alter the feedback mechanisms and the way the body responds.



Stres ni le občutek.

Je merljiv fiziološki odziv, ki vpliva na življenje in delovanje ljudi.

62%

of people reported experiencing stress in the past year to an extent that affected their daily lives.²

Prolonged activation of the stress response is associated with



poorer cognitive function



poorer sleep



metabolic disorders

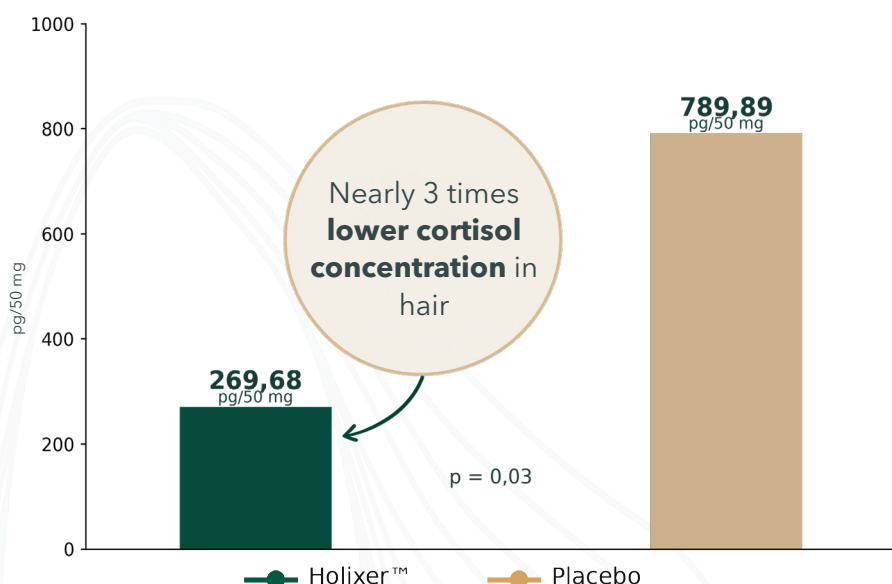


cardiovascular problems

Effect on stress and the cortisol response

Holixer™ is a standardized extract of holy basil (*Ocimum tenuiflorum*), clinically studied in **adults with elevated levels of perceived stress**. The study evaluated its effects on **perceived stress, sleep quality and the physiological stress response, including cortisol**.¹

Cortisol concentration in newly grown hair



RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

- 100 participants** with elevated stress levels
- 250 mg/day**
- 8 weeks**
- No reported serious adverse events**

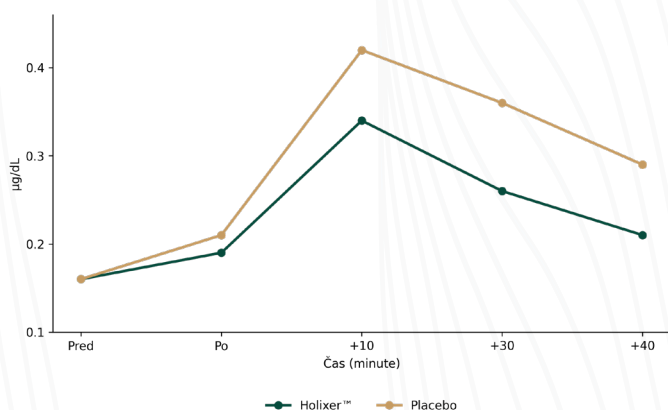
After 8 weeks of Holixer™ supplementation, the cortisol concentration in the newly grown hair segment was statistically significantly lower compared with placebo (p = 0.03).¹

Response to acute stress (MAST)¹

To assess the response to acute stress, after 8 weeks of supplementation participants were exposed to the Maastricht Acute Stress Test (MAST). The physiological stress response was monitored objectively, while perceived stress was assessed using a visual analogue scale (VAS). Participants rated their current level of stress before the MAST and then at 10, 20, 30 and 40 minutes after the stressor.¹

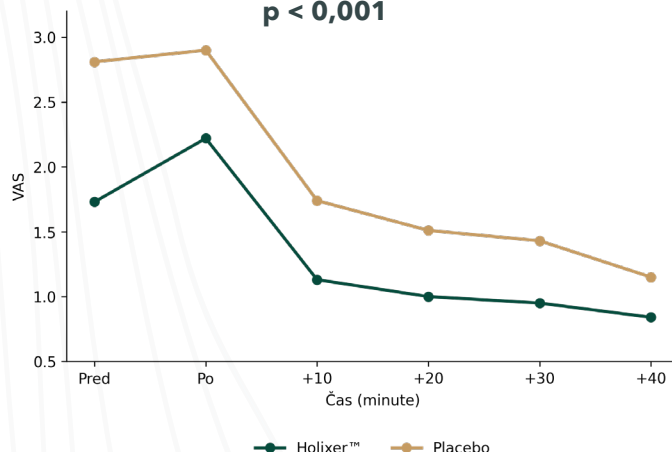
After 8 weeks of Holixer™ supplementation, statistically significant differences between the groups in response to the MAST were observed in salivary cortisol, salivary α -amylase, systolic and diastolic blood pressure, and subjective stress scores.¹

Salivary cortisol p=0,001



In response to acute stress, a statistically significant difference between the groups was observed in salivary cortisol (p = 0.001).

Subjective stress score (VAS) p < 0,001



During acute stress, participants in the Holixer™ group reported lower subjective stress scores compared with the placebo group (p < 0.001).¹

Clinical study of stress-related symptoms

Lactium® is a **bioactive α S1-casein hydrolysate**, obtained through the enzymatic hydrolysis of milk proteins. It contains bioactive peptides, among which α -casozepine has been particularly well studied. Lactium® was **clinically studied for its effects on stress-related symptoms and specific aspects of sleep quality**.

RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSSOVER STUDY



63 women



150 mg/day



30 days



Excellent safety profile

IMPROVEMENT IN STRESS-RELATED SYMPTOMS

After **30 days**, participants with pronounced symptoms at baseline showed a **statistically significantly greater improvement compared with placebo in five areas**.³



COGNITIVE SYMPTOMS

64,8 % improvement

placebo 36,7 %



DIGESTIVE SYMPTOMS

66,1 % improvement

placebo 36,6 %



CARDIOVASCULAR SYMPTOMS

48,0 % improvement

placebo 35,5 %



EMOTIONAL SYMPTOMS

43,8 % improvement

placebo 23,5 %



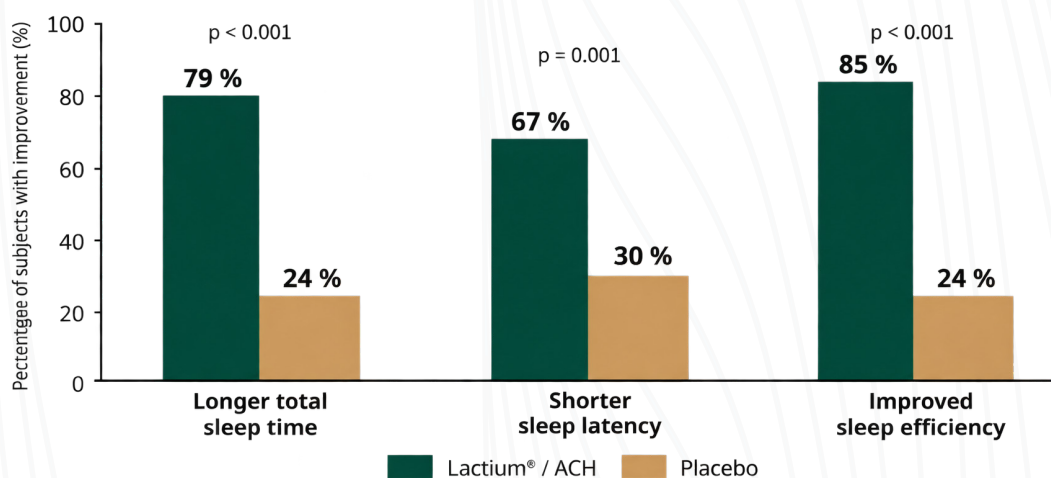
SOCIAL FUNCTIONING

36,7 % improvement

placebo 22,5 %

IMPROVED SLEEP QUALITY

In a clinical study in adults with mild to moderate sleep disturbances, 4 weeks of α S1-casein hydrolysate supplementation improved several subjective and objective sleep parameters, including total sleep time, sleep latency and sleep efficiency.



LONGER SLEEP TIME
79 % improvement



IMPROVED SLEEP EFFICIENCY
85 % improvement



SHORTER SLEEP LATENCY
67 % improvement

The power of Cortisen® lies in its carefully designed formula

Cortisen® is a food supplement developed to support the nervous system and psychological function during periods of increased mental strain. Its formula combines three scientifically studied active ingredients – Holixer™, Lactium® and L-theanine – together with B-complex vitamins, zinc and selenium.

The selected active ingredients complement each other through different mechanisms associated with the physiological and psychological response to stress. Particular emphasis is placed on the cortisol response, neurotransmitter signalling, maintaining inner calm and cognitive performance.

Three key active ingredients – support during stress

The stress response involves several interconnected physiological and neurological processes, which is why individual active ingredients act at different levels of the body. Holixer™, Lactium® and L-theanine have been clinically studied in relation to stress, sleep, relaxation and the cortisol response.

Their actions complement each other at several levels – from regulation of the stress and cortisol response to processes associated with relaxation, attention and cognitive function.



Holixer™

48 % reduction in symptoms of restlessness

in a clinical study¹



Lactium®

17,6 % reduction in serum cortisol

in a clinical study²



L-theanine

42,4 % reduction in salivary cortisol

in a clinical study³

Effects of the active ingredients

Holixer™	Standardised extract of <i>Ocimum tenuiflorum</i> , clinically studied for perceived stress, mood, sleep and acute and long-term cortisol response .
Lactium®	Bioactive α S1-casein hydrolysate containing bioactive peptides, among which α -casozepine has been particularly well studied. Research indicates an association with the GABAergic system and the body's response to stress .
L-theanine	A non-protein amino acid studied for its effects on neurophysiological processes associated with stress response, relaxation, attention and cognitive function .
Vitamins B1, B6, B12 and folate	Contribute to normal psychological function and normal functioning of the nervous system. Vitamins B6, B12 and folate contribute to the reduction of tiredness and fatigue .
Zinc	Contributes to normal cognitive function and to the protection of cells from oxidative stress .
Selenium	Contributes to the protection of cells from oxidative stress.

L-theanine

L-theanine is a non-protein amino acid naturally found mainly in the leaves of the tea plant (*Camellia sinensis*). Clinical studies have examined its effects on **stress, relaxation, sleep quality and cognitive function**. Its action is associated with effects on processes in the central nervous system, while helping to maintain a state of **relaxed alertness without pronounced drowsiness**.

Clinical study on stress, sleep and cognitive function

After four weeks of L-theanine supplementation, participants showed a **statistically significant reduction in symptoms of anxiety and irritability, as well as an improvement in sleep quality**. Improvements were also observed in certain sleep parameters, including sleep onset latency and sleep disturbances, compared with placebo.⁵

RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSSOVER STUDY



32 adults



200 mg/days



4 weeks



No reports of serious adverse events

RESPONSE TO ACUTE STRESS⁶

In a randomised, triple-blind, placebo-controlled crossover study, 16 healthy adults with moderate perceived stress received a single dose of **200 mg L-theanine** or placebo. **To induce acute stress, participants completed mental arithmetic tests, followed by measurements of salivary cortisol and EEG brain activity, as well as other physiological and subjective markers of the stress response.**⁶



SALIVARY CORTISOL
42,4 % reduction

1 hour after intake⁶



BRAIN ALPHA ACTIVITY
greater increase in alpha activity

3 hours after intake⁶



RELAXED ALERTNESS
Increased alpha activity associated with relaxation without drowsiness⁶

RELAXED ALERTNESS⁶

Increased alpha activity is associated with a **state of relaxation without drowsiness**. In the study, a single dose of L-theanine **increased frontal and overall alpha activity** and at the same time **resulted in a greater reduction in salivary cortisol compared with placebo.**⁶

Reference

- 1 Lopresti AL, Smith SJ, Metse AP, Drummond PD. A randomized, double-blind, placebo-controlled trial investigating the effects of an *Ocimum tenuiflorum* (Holy Basil) extract (Holixer™) on stress, mood, and sleep in adults experiencing stress. *Front Nutr.* 2022;9:965130. doi:10.3389/fnut.2022.965130.
- 2 Ipsos. World Mental Health Day Report 2024. Global survey across 31 countries. 2024.
- 3 Kim JH, Desor D, Kim YT, Yoon WJ, Kim KS, Jun JS, et al. Efficacy of α s1-casein hydrolysate on stress-related symptoms in women. *Eur J Clin Nutr.* 2007;61(4):536-541. doi:10.1038/sj.ejcn.1602553.
- 4 Saint-Hilaire Z, Messaoudi M, Desor D, Kobayashi T. Effects of a bovine alpha S1-casein tryptic hydrolysate (CTH) on sleep disorder in Japanese general population. *Open Sleep J.* 2009;2:26-32. doi:10.2174/1874620900902010026.
- 5 Hidese S, Ogawa S, Ota M, Ishida I, Yasukawa Z, Ozeki M, Kunugi H. Effects of L-theanine administration on stress-related symptoms and cognitive functions in healthy adults: a randomized controlled trial. *Nutrients.* 2019;11(10):2362. doi:10.3390/nu11102362.
- 6 Evans M, McDonald AC, Xiong L, Crowley DC, Guthrie N. A randomized, triple-blind, placebo-controlled, crossover study to investigate the efficacy of a single dose of AlphaWave® L-theanine on stress in a healthy adult population. *Neurol Ther.* 2021;10(2):1061-1078. doi:10.1007/s40120-021-00284-x.