natural®
REMEDIES

HOLIXER®

Stress Less | Sound Sleep | Wake Fresh

Clinically validated extract of Holy Basil

About Stress & Sleep: A Global Story of a Growing Need

Sleep is one of the body's most powerful biological reset mechanisms. It drives cellular repair, strengthens brain plasticity, supports emotional balance, and fuels cognitive performance. Yet despite its central role in human health, sleep is becoming increasingly fragile. **Globally, 1 in 3 adults struggle with sleep,** and for more than half, the root cause is **stress and anxiety,**[1,2] highlighting how deeply intertwined these challenges have become. Stress disrupts sleep, and poor sleep heightens stress a self-reinforcing cycle now reshaping consumer behaviour, clinical strategies, and the wellness market.

A Market Growing as Fast as the Problem

Sleep Supplement Market [3]

$7.5 billion

Market valued at USD 7.5 billion in 2025, is projected to reach USD 12.8 billion by 2035 (CAGR 5.4%).
The natural segment leads with 58.4% share, driven by consumer preference for herbal and plant-based formulations.

Stress Support Supplements Market[4]

$5.67 billion

Market valued at USD 5.67 billion in 2024, is expected to nearly double to USD 10.25 billion by 2033 at a CAGR of 7.25%.

These trends reflect not just market growth but a global unmet need for holistic solutions that break the stress–sleep cycle and restore balance.

A Vicious Circle of Stress & Sleep

Stress activates the Hypothalamic–Pituitary–Adrenal (HPA) axis, raising cortisol to help manage immediate challenges. When this response becomes chronic, elevated cortisol disrupts circadian rhythms, making it harder to fall or stay asleep. Disrupted sleep then alters regulation of neuropeptides governing the sleep–wake cycle, increasing emotional reactivity and reducing resilience.[5] This deepening loop where stress worsens sleep and poor sleep amplifies stress carries long-term consequences, including weakened immunity, cognitive and mood disturbances, metabolic issues, and accelerated aging. Consumers increasingly seek solutions that not only promote sleep but break this cycle to restore long-term balance.

Navigating the Stress & Sleep Supplement Landscape

For decades, pharmaceuticals such as benzodiazepines, Z-drugs, and antidepressants have dominated treatment. While effective acutely, they carry risks of dependence, tolerance, cognitive impairment, and disrupted sleep architecture.[6,7] This has opened the door to non-habit-forming alternatives. Botanicals like standardized saffron extracts show benefits for mild, stress-linked sleep issues, yet their effects on micro-structural, unfragmented and restorative sleep are limited. Valerian faces challenges with extract consistency due to unstable constituents like valepotriates.[8]

Melatonin remains the most recognized natural option for circadian alignment, but absorption variability, drug interactions, and inconsistent dosing raise concerns, and long-term use may diminish effectiveness. [9,10] Formulators are therefore moving toward low-dose melatonin + botanical blends supported by robust safety data. Also, magnesium aid relaxation through N-Methyl-D-Aspartate (NMDA) regulation and Gamma-Aminobutyric Acid (GABA) enhancement, though evidence is constrained by deficiency variability and digestive effects from certain salts. [11,12]

These insights highlight increasing demand for botanical actives with precise standardization, consistent pharmacodynamics, and validated safety.

A Broader Industry Shift

The sleep sector is moving from sedative-based products to neuroscience-informed solutions that enhance sleep quality, not just duration. Research now emphasizes sleep microarchitecture, with CAP-A1 emerging as a key marker of stable, restorative sleep.[13] By supporting these microstructural patterns, next-generation ingredients can enhance cognition, emotional balance, and overall well-being. Many also modulate stress pathways like the HPA axis, reinforcing the connection between stress and sleep. As science advances, standardized botanicals such as holy basil are demonstrating the potential of natural, evidence-based solutions for unfragmented sleep that culminates in restoring physiological and mental health benefits and next day optimal functioning.

HPA axis: Hypothalamic–Pituitary–Adrenal axis; NMDA: N-Methyl-D-Aspartate; GABA: Gamma-Aminobutyric Acid

Exploring The Holy Basil Space

As next-generation natural solutions reshape the stress and sleep category, Holy Basil *(Ocimum tenuiflorum)* is emerging as a standout botanical. Traditionally revered in Ayurveda for calming the mind and enhancing resilience, it is now being recognized by modern science for its influence on the HPA axis, sympathetic activity, and sleep pathways. This positions Holy Basil uniquely at the intersection of tradition and biology addressing both stress and sleep together. With global demand rising for effective natural solutions, Holy Basil offers a compelling answer. Holixer® leads this space by bringing scientific rigor, standardized actives, and clinically validated outcomes to this centuries-old adaptogen.

Award Winning Holixer® Advantage: Precision Science

Holixer® stands apart because the discovery is rooted in our unique, proprietary Bioactive Optimization Technology (B.O.T)™. This technology ensures that Holixer® is standardized to Ocimum Bioactive Complex (≥5% w/w by HPLC) to ensure consistent levels of five key phytoactive compounds. As a clinically validated extract, Holixer® opens a new frontier in stress and sleep management bringing modern science to a revered traditional botanical.

Our Unique Strengths

Innovative
Developed with B.O.T technology to maximize efficacy

Clinically Proven
Backed by clinical trials

Safe
Designed for daily use and non-habit forming

Innovative: Bioactive Optimization Technology (B.O.T)™

Natural Remedies leverages its proprietary, Bioactive Optimization Technology (B.O.T.)™. This state-of-the art technology combines the principles of chemistry and biological sciences to deliver a bioactive optimized extract, characterized by high bioactivity at low dose. The approach emcompasses full spectrum activity, ensuring the delivery of an ingredient with enhanced efficacy, robust safety profile and with significant impact.

Natural Remedies follows two phase process in this endeavour. The initial discovery phase involves designing multiple fractions, guided by a new product need. These fractions may encompass diverse characteristics, such as polar or nonpolar properties or hydro actives components, etc. Approximately 50 to 60 leads are generated, subsequently subject to rigorous screening, utilizing mathematical models, predictive screening methodologies and biological studies, to generate a comprehensive dataset. This dataset comprises information pertaining to the effects of individual fractions and their combinations, predictive effects of these combinations, and the interactive effects of specific phytoactive fractions. The subsequent optimization phase focuses on refining the identified lead. This is achieved through an iterative process involving the integration of phytochemical and biological investigations, culminating in a bioactive-optimized extract that exhibits high and targeted bioactivity at a reduced dose. It uses intelligent combinations of fractions to achieve synergistic actions to form Ocimum Bioactive Complex (OBC). The key phytochemicals in Holy Basil are optimized for maximum effectiveness. This process has yielded Holixer® a standardized Holy Basil extract demonstrating clinical efficacy at a dose of 250mg per day.

Phytochemistry of Ocimum Bioactive Complex (OBC)

The key phytochemical compounds found in holy basil are rabdosiin, rosmarinic acid, luteolin-7-O-glucuronide, apigenin-7-O-beta-glucuronide, and ociglycoside-I ≥ 5% w/w by HPLC.

Holixer®: Receptor Functional Assay and In-Silico Evidence Demonstrating Efficacy

Advanced in silico molecular docking studies confirm that Holixer®'s five optimized phytoactives exhibit strong and selective binding affinity to key neurological receptors involved in stress and sleep regulation including Galanin, MCH, Melatonin, and Orexin 1 & 2. These findings indicate a meaningful potential for Holixer® to modulate central pathways governing stress response and sleep architecture.

Complementary receptor functional assays further substantiate these observations, demonstrating that Holixer® functions as an agonist on sleep-promoting pathways and an antagonist on arousal-associated pathways. Collectively, this integrated evidence base provides strong scientific support for Holixer®'s capacity to facilitate sleep initiation, promote restorative sleep quality, and attenuate hyperarousal and stress signalling.

Holixer®: Preclinical Validation of Safety and Stress-Relieving Potential

Preclinical research published in PLOS One demonstrated Holixer®'s antistress activity using two in vivo models: the swim endurance test in mice and the forced swim test in rats. Holixer® increased swim endurance, reduced corticosterone elevation, supported by in vitro studies showing inhibition of cortisol release and significant CRF1 receptor antagonism.[14]

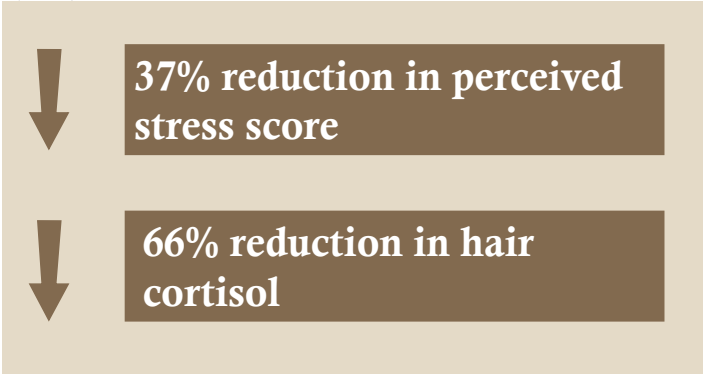
Its safety profile, published in Drug and Chemical Toxicology, confirmed no mutagenic or clastogenic effects across bacterial, in vitro, and in vivo assays. Holixer was also shown to be safe in acute toxicity studies up to 5 g/kg in rats.[15]

Together, these findings establish Holixer® as a non-genotoxic, well-tolerated extract with robust preclinical evidence supporting its role in safe, effective stress management.

Clinical evidence: A Hallmark of Scientific Excellence

In a randomized, double-blind, placebo-controlled clinical study, Holixer® was evaluated for its impact on stress and sleep in one hundred healthy adults experiencing moderate stress. Participants received 250 mg of Holixer® daily for eight weeks. Over the course of the study, Holixer® demonstrated meaningful benefits across everyday stress, acute stress response, sleep quality, and overall well-being.

Everyday stress was assessed using both the perceived stress scale and hair cortisol, a robust biomarker of long-term stress. Participants supplemented with Holixer® showed a clear reduction in psychological and biochemical markers of stress, including a 37% reduction in perceived stress scores from baseline and a 66% decrease in hair cortisol compared with placebo, underscoring Holixer®'s ability to manage



To evaluate resilience under acute stress, the Maastricht Acute Stress Test (MAST) was employed. This standardized protocol alternates five cycles of hand immersion in freezing water with mental arithmetic tasks to induce both physical and psychological stress. Stress markers including salivary cortisol, salivary alpha-amylase, and blood pressure were recorded to quantify stress reactivity. Individuals receiving Holixer® exhibited a noticeably calmer and more controlled response, with rapid relief within just 10 minutes, accompanied by significant reductions in salivary cortisol, and lower sympathetic activation.These results highlight Holixer®'s capacity not only to reduce chronic stress but also to enhance the body's ability to manage acute stress challenges.

Equally compelling improvements were observed in sleep outcomes. Participants taking Holixer® experienced marked benefits on the Athens Insomnia Scale, achieving a 48% greater improvement than placebo, while objective Fitbit® measurements confirmed significant gains in sleep efficiency. These enhancements in restorative sleep translated into broader improvements in daily functioning. PROMIS-29 scores reflected meaningful increases in quality of life, including 28% reduction in fatigue, 36% reduction in anxiety, and 30% reduction in sleep disturbance.[16]

Taken together, the findings demonstrate that Holixer® delivers clinically validated dual action effectively reducing stress while restoring healthy sleep, with benefits evident across subjective assessments, & objective biomarkers.

Sleep Structure and Stability: A Closer Look

While improvements in sleep scores, biomarkers, and wearable data are encouraging, truly unfragmented sleep can only be understood by looking deeper into the architecture and stability of sleep itself. Our nightly sleep cycles, the macro-architecture, tell us when we sleep and for how long, but they don't fully explain how restorative that sleep truly is.

The real essence of deep, restorative sleep lies in its micro-architecture, particularly the Cyclic Alternating Pattern (CAP) a natural EEG rhythm that appears during NREM sleep. CAP reflects the brain's moment-to-moment ability to maintain stability as it moves through different depths of sleep. Each CAP cycle alternates between a brief activation (Phase A) and a return to deeper, more stable sleep (Phase B).

Not all activations are the same. A1 events are gentle, slow-wave–rich activations that actually reinforce deep, unfragmented sleep, while A2 and A3 events mark instability and fragmentation. A night dominated by A1 activity is a night of consolidated, restorative sleep; a night with more A2 or A3 activity feels broken even if total sleep time appears normal.

A higher proportion of A1 subtypes is therefore recognized as a key hallmark of healthy, unfragmented sleep. Boosting A1 activity is considered a leading neurophysiological target for any approach that aims to restore natural sleep architecture, rather than simply induce sedation or extend total sleep time.

Seen through this lens, Holixer®'s clinical outcomes gain deeper relevance. By improving both subjective sleep quality and objective sleep efficiency and aligning with the principles that define sleep stability at the micro-architectural level Holixer® demonstrates the potential to support sleep that is not only longer, but genuinely more stable and more restorative.[17-20]

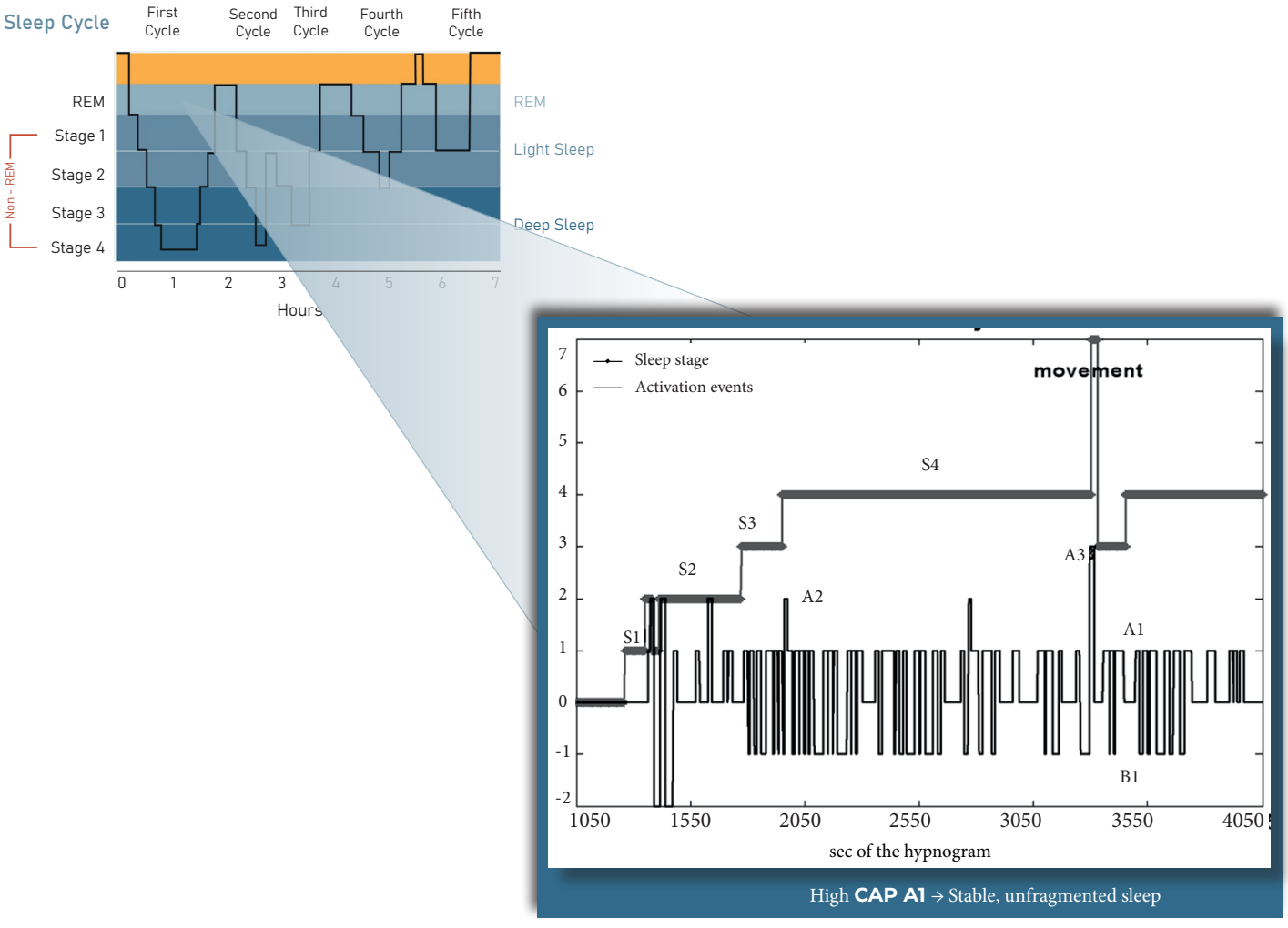


Image courtesy: https://www.researchgate.net/figure/Hypnogram-and-characteriztion-of-CAP-microstruture-time-series-ie_fig1_230599496

A Global First: Sleep Microarchitecture

Holixer® marks a significant milestone in sleep science by becoming the first botanical ingredient globally to demonstrate measurable improvement in sleep microarchitecture unfragmented dimension of sleep validated through gold-standard polysomnography (PSG).

In an independent clinical study involving seventy adults, participants received 250 mg of Holixer® daily for eight weeks. The findings were remarkable: Holixer® produced a 95% improvement in CAP A1 rate, the marker most closely associated with stable, deep, unfragmented NREM sleep. An increase in A1 activity is widely recognized as the clearest indicator of improved sleep continuity, enhanced stability, and stronger restorative capacity at a neurophysiological level.

This shift toward higher A1 dominance translates into fewer night-time awakenings, smoother transitions between sleep stages, and deeper recovery processes that help support cognitive, emotional, and physical restoration.

Actigraphy provided complementary evidence. Participants experienced faster sleep onset, fewer disturbances through the night, and a more consistent sleep–wake rhythm. These improvements align closely with what consumers seek today sleep that is not only longer, but genuinely restorative.

Holixer® also demonstrated meaningful benefits on the Insomnia Severity Index (ISI). Participants exhibited a 50% improvement in sleep quality from baseline. Taken together, these findings establish Holixer® as a new benchmark in natural restorative sleep solutions. [21]

95%
improvement in CAP A1 rate

50%
improvement in sleep quality from baseline

Holixer® Mechanism of Action:

RESET: The Stress Axis

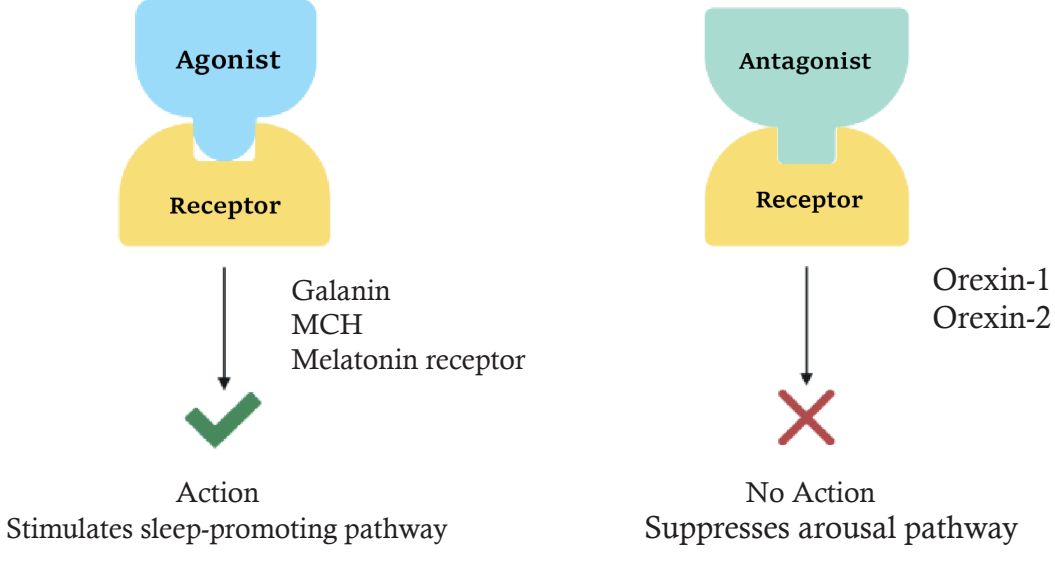
Dual-R Action

RESTORE: The Natural Sleep–Wake Rythm

Chronic stress disrupts both the HPA axis and the Sympathetic Nervous System. Holixer® helps reset these systems by inhibiting CRF1 receptor activity, reducing cortisol and lowering sympathetic drive evident through decreased salivary α-amylase and more stable cardiovascular responses during stress. Together, these effects help shift the body from a state of hyperarousal to a more regulated and adaptive stress response.

Holixer® then restores sleep physiology through targeted modulation of key neuropeptide receptors. By agonising Galanin, MCH, and Melatonin receptors and simultaneously antagonising Orexin-1 and Orexin-2, it strengthens sleep-promoting pathways while suppressing arousal. Clinically observed improvements in CAP A1 activity, sleep continuity, and overall sleep quality reflect this deep, restorative influence on sleep microarchitecture.

Through this integrated RESET and RESTORE mechanism, Holixer® addresses both the cause and the consequence of stress-related sleep disturbances providing a scientifically coherent and clinically validated pathway to calmer days and more restorative nights.



MCH: Melanin-Concentrating Hormone

Holixer®: A Sustainably Crafted Ingredient Backed by HerbSecure™

Holixer® is crafted through HerbSecure™, our commitment to ethical sourcing, farmer empowerment, and environmental stewardship. Grown on partner farms using regenerative practices, Holixer® protects soil health, conserves water, and supports biodiversity while ensuring farmers fair pricing and assured offtake. Every batch is fully traceable to its origin, guaranteeing purity, authenticity, and trust. By cultivating responsibly not depleting natural resources Holixer® delivers a clinically proven ingredient that supports people, the planet, and the future of botanical wellness.

Global Regulatory Advantage

Holixer® is built on a strong global regulatory foundation, ensuring compliance across key international markets. With Self-Affirmed GRAS in the US, Complementary Medicine in ANZ, and Korea MFDS IAFF approval, Holixer® is ready for seamless global adoption. Our commitment is simple and steadfast: Holixer® will continue to meet the highest regulatory standards wherever our partners choose to take it.

Award-Winning Excellence

Holixer® has been honoured as Ingredient of the Year:Mind & Mood at the NutraIngredients USA Awards 2025, and was named the First Runner-Up in the Innovation Zone at Vitafoods India 2025, recognizing its robust clinical science and leadership in botanical stress and sleep solutions.

Holixer®: Holistic Support for Stress Management & Restorative Sleep

In 10 minutes*
Rapid relief from acute stress

Within 2 weeks
Marked reduction in stress

Under stress conditions
Controls stress-induced blood pressure spikes

Supports restorative sleep
50% improvement in sleep quality
95% reduction in sleep disturbances (based on CAP A1)
60% faster sleep onset

Supports next-day functioning within 4 weeks
Wake up feeling restored and refreshed

Designed for daily use
Non-habit forming, and with zero fading effect over time

*On regular intake

HOLIXER®

Stress Less | Sound Sleep | Wake Fresh

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