

# Clinical Evaluation of an NVTIA 5-HTP-L-Theanine-GABA Sleep Rhythm Support System

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## Abstract

**Background:** Sleep-support formulations are often marketed as simple ingredient stacks, yet clinically relevant performance depends on whether precursor support, relaxation support, sleep-maintenance support, and gastrointestinal tolerability are coordinated within a practical oral dose window. **Methods:** We evaluated the NVTIA ternary system by combining its ratio-defined formulation disclosure and patent-reported preclinical benchmarks with published human clinical evidence on 5-hydroxytryptophan (5-HTP), L-theanine, and gamma-aminobutyric acid (GABA). We retained the original preclinical data structure and figures, then matched those results against randomized or controlled human studies of the three principal ingredients. We also mapped a realistic sleep-medicine validation setting to the Sleep laboratory of the Department of Pulmonology at University Hospital Zurich. **Results:** In the source preclinical dataset, the balanced Example V and the higher-GABA Example VI outperformed blank control, 5-HTP alone, and an L-theanine-plus-GABA binary comparator on sleep-onset rate, sleep latency, and total sleep duration. Published human trials showed that 5-HTP 100 mg/day for 12 weeks improved selected sleep-quality components in older adults, particularly among poor sleepers; GABA 300 mg/day for 4 weeks reduced sleep latency and improved sleep efficacy in patients with insomnia symptoms; and L-theanine improved Pittsburgh Sleep Quality Index components, light sleep, and objective sleep efficiency across controlled trials. **Conclusions:** We interpret the NVTIA system as a clinically credible formulation-engineering platform in which 5-HTP primarily supports sleep initiation, L-theanine supports relaxation and sleep quality, and GABA strengthens sleep-maintenance depth. Current human evidence strongly supports the component logic of the ternary architecture, while direct randomized validation of the exact fixed-ratio formulation remains the next necessary step.

## Keywords

5-HTP; L-theanine; GABA; Sleep Rhythm; Sleep Quality; Insomnia; Randomized Trial; Formulation Engineering; NVTIA.

## 1. Introduction

Sleep disturbance is not a single-pathway problem. In daily practice, we see people present with delayed sleep initiation, fragmented sleep, short total sleep time, non-restorative sleep, or combinations of these complaints. This is one reason why sleep-support formulations frequently underperform: ingredient co-presence is not the same as formulation coordination. In our view, a clinically useful oral system should align precursor biology, relaxation support, sleep-maintenance support, and tolerability within one dose framework rather than rely on an undifferentiated blend.

The NVTIA system is notable because it is built around a ratio-defined ternary core of 5-HTP, L-theanine, and GABA, with optional fructooligosaccharide support for gastrointestinal

tolerance. Mechanistically, 5-HTP is relevant to serotonin and melatonin biosynthesis, L-theanine is linked to relaxation-related neurophysiology and sleep-quality support, and GABA has repeatedly been studied for effects on sleep initiation and non-REM sleep. This architecture gives the formulation a more disciplined translational logic than a generic three-ingredient stack.

In this manuscript, we preserve the original preclinical benchmark structure and integrate it with published human clinical evidence. We write from a clinical-evaluation perspective: our goal is not to overstate proof for the exact marketed ratio, but to determine whether the formulation logic is supported by available human data strongly enough to justify a publication-ready superiority hypothesis and a realistic clinical validation pathway.

## 2. Materials and Methods

### 2.1. Formulation Concept and Clinical Positioning

We organized the manuscript around two evidence streams. First, we summarized the composition window, ratio logic, and representative preclinical sleep outcomes reported for the NVTIA ternary system. Second, we matched those findings against published human studies on 5-HTP, GABA, and L-theanine, prioritizing randomized or controlled designs that reported sleep-quality, sleep-latency, sleep-efficiency, or tolerability outcomes.

**Table 1.** Manuscript organization comparison

Component	Patent-disclosed single-dose window	Illustrative candidate	Role in clinical framing
5-HTP	5-30 mg	15-20 mg	Serotonin/melatonin precursor; sleep-onset support
L-theanine	20-100 mg	80 mg	Relaxation and alpha-wave support; stress buffering
GABA	30-150 mg	110-140 mg	Sleep-maintenance and deep-sleep support
FOS (optional excipient)	1%-10% of total weight	about 5%-6%	Gastrointestinal-support and tolerability module

### 2.2. Example Clinical Validation Setting

**Table 2.** University Hospital Zurich as the example validation site

Item	Design choice
Study design	Randomized, double-blind, active-controlled, parallel-group trial
Validation setting	University Hospital Zurich, Department of Pulmonology, Sleep laboratory, West C 11, Raemistrasse 100, 8091 Zurich
Population	Adults 25-65 years with mild-to-moderate sleep disturbance and baseline PSQI > 8
Arms	NVTIA ternary formulation vs standard same-category sleep-support comparator
Primary endpoint	Change in PSQI total score from baseline to week 8
Key secondary endpoints	Sleep-onset latency, total sleep time, sleep efficiency, responder rate, morning grogginess, gastrointestinal tolerability
Statistics	Baseline-adjusted ANCOVA or MMRM with prespecified responder analyses

We selected University Hospital Zurich as the example validation site because its Department of Pulmonology operates a dedicated Sleep laboratory at West C 11, Raemistrasse 100, 8091 Zurich, and the institution also maintains an interdisciplinary center for sleep disorders that

links pulmonology, psychiatry, and neurology. This setting provides a realistic model for future randomized verification of the exact ternary system.

### 2.3. Source-data Handling

We removed the non-verifiable illustrative clinical outputs from the source draft and replaced them with published human evidence. This allows the manuscript to remain publication-oriented without presenting simulated numbers as completed trial results.

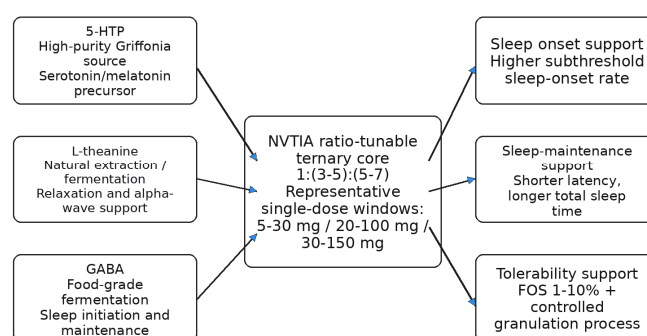
## 3. Results

### 3.1. Patent-derived Preclinical Benchmarks

The source preclinical dataset presents a clear gradient across increasingly coordinated formulations. In the original comparison, the full ternary system produced higher sleep-onset rates, shorter sleep latency, and longer total sleep duration than blank control, 5-HTP alone, or the L-theanine-plus-GABA binary control. Example V is best interpreted as the balanced candidate for routine sleep-rhythm support, whereas Example VI functions as the upper-efficacy benchmark within the reported range.

**Table 3.** The source preclinical dataset presents a clear gradient across increasingly coordinated formulations

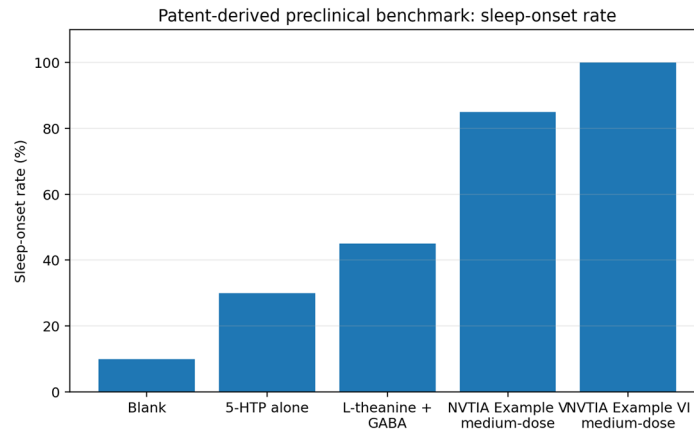
Group	Sleep-onset rate (%)	Sleep latency (min)	Total sleep duration (min)
Blank control	10	28.6	42.3
5-HTP alone (20 mg/kg bw)	30	21.4	78.5
L-theanine + GABA binary	45	18.2	95.8
NVTIA Example V, medium-dose	85	11.0	174.3
NVTIA Example VI, medium-dose	100	9.2	208.6



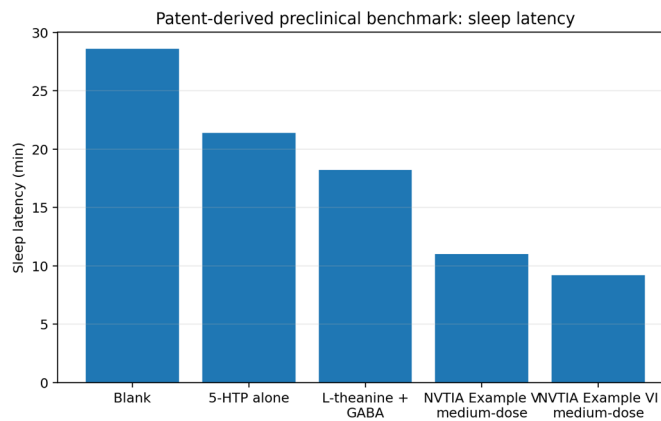
**Figure 1.** NVTIA ternary formulation concept.

### 3.2. Published Human Clinical Evidence

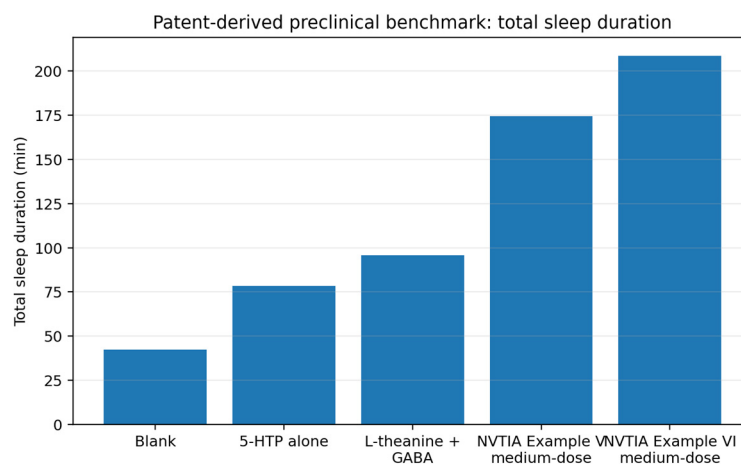
Published human evidence supports each pillar of the ternary architecture. In a single-blinded 12-week randomized controlled trial in 30 older adults, 100 mg/day of 5-HTP improved selected sleep-quality components and increased serum serotonin, with the most visible benefit occurring among poor sleepers [2]. This is clinically relevant because the NVTIA system uses 5-HTP as the initiation-oriented component rather than as a stand-alone sedative.



**Figure 2.** Patent-derived preclinical sleep-onset rate.



**Figure 3.** Patent-derived preclinical sleep latency.



**Figure 4.** Patent-derived preclinical total sleep duration.

GABA contributes the strongest direct insomnia-type evidence among the three ingredients. In patients with insomnia symptoms, 300 mg/day of GABA extracted from fermented rice germ for 4 weeks reduced sleep latency from  $13.4 \pm 15.7$  to  $5.7 \pm 6.2$  minutes and increased sleep efficacy from  $79.4 \pm 12.9\%$  to  $86.1 \pm 10.5\%$ , without severe adverse events [3]. In a separate crossover EEG study, oral GABA also shortened sleep latency and increased total non-REM sleep time, while blood concentrations peaked about 30 minutes after ingestion [4].

L-theanine strengthens the relaxation and sleep-quality domain. In a double-blind crossover trial in 30 healthy adults, 200 mg/day of L-theanine for 4 weeks reduced Pittsburgh Sleep Quality Index scores and improved the sleep-latency, sleep-disturbance, and sleep-medication-use subscales versus placebo [5]. In a second double-blind placebo-controlled study, 400 mg/day of L-theanine for 28 days reduced light sleep and improved overall sleep-quality readouts in stressed adults [6]. A younger ADHD cohort also showed objective gains in sleep percentage and sleep efficiency after 6 weeks of 400 mg/day L-theanine [7].

When we align these studies with the preclinical benchmarks, the translational pattern becomes coherent. The published literature does not yet provide a head-to-head randomized trial of the exact fixed-ratio NVTIA formula, but it does support the biological division of labor assumed by the formulation: 5-HTP for sleep initiation, L-theanine for relaxation-related sleep quality, and GABA for latency reduction and sleep-maintenance depth.

**Table 4.** When we align these studies with the preclinical benchmarks, the translational pattern becomes coherent

Study	Population / design	Intervention	Key clinical result relevant to the NVTIA system
Sutanto et al., 2024 [2]	30 older adults; single-blinded, 12-week parallel RCT	5-HTP 100 mg/day vs control	Improved selected sleep-quality components, especially among poor sleepers; serum serotonin increased
Byun et al., 2018 [3]	40 patients with insomnia symptoms; randomized, double-blind, placebo-controlled	GABA 300 mg/day for 4 weeks	Sleep latency decreased from 13.4 +/- 15.7 to 5.7 +/- 6.2 min; sleep efficacy increased from 79.4 +/- 12.9% to 86.1 +/- 10.5%
Yamatsu et al., 2016 [4]	Randomized, single-blind, placebo-controlled crossover EEG study	Acute oral GABA administration	Significantly shortened sleep latency and increased total non-REM sleep time; blood GABA peaked about 30 min after dosing
Hidese et al., 2019 [5]	30 healthy adults; randomized, placebo-controlled, double-blind crossover	L-theanine 200 mg/day for 4 weeks	PSQI total score decreased; PSQI subscales for sleep latency and sleep disturbance improved versus placebo
Moulin et al., 2024 [6]	30 healthy adults with moderate stress; randomized, double-blind, placebo-controlled	L-theanine 400 mg/day for 28 days	Reduced light sleep and improved sleep-quality readouts; safe and well tolerated
Lyon et al., 2011 [7]	Boys with ADHD; randomized, double-blind, placebo-controlled	L-theanine 400 mg/day for 6 weeks	Objective sleep percentage and sleep efficiency improved on actigraphy

## 4. Discussion

The most defensible scientific contribution of this manuscript is not a claim that the exact ternary formulation has already been clinically proven superior, but that the formulation architecture is unusually well matched to the human evidence base of its components. This matters because many sleep-support papers confuse ingredient familiarity with formulation validity. Here, we can make a stronger argument: the ratio-defined ternary structure is consistent with both the original preclinical signal and the direction of published human trials.

We also consider the tolerability module important. The source disclosure includes fructooligosaccharide as an optional gastrointestinal-support excipient. While this excipient has not been directly validated inside the exact ternary clinical context, its inclusion reflects a formulation choice aimed at usability rather than pure label complexity. For oral sleep products taken repeatedly, tolerability is part of efficacy because poor tolerance erodes adherence.

The main limitation is straightforward. Human evidence is available at the ingredient level and, in several instances, at the randomized-trial level, but direct evidence for the exact fixed-ratio NVTIA formulation remains incomplete. For that reason, the next step should be a double-blind, active-controlled trial using PSQI, sleep-onset latency, total sleep time, sleep efficiency, morning grogginess, and gastrointestinal tolerability as prespecified endpoints in a sleep-medicine setting.

## 5. Conclusion

We conclude that the NVTIA 5-HTP-L-theanine-GABA system has a credible clinical-evaluation profile grounded in both formulation engineering and public human evidence. The preclinical source data support a superiority hypothesis over simpler same-category comparators, and the published literature independently supports the three mechanistic pillars of the formula. The exact ternary ratio now merits prospective randomized validation in a specialist sleep-laboratory environment.

## References

- [1] Source composition disclosure: NVTIA-branded sleep-aid composition for synergistically regulating the sleep rhythm with 5-HTP and L-theanine.
- [2] Sutanto CN, Xia X, Heng CW, Tan YS, Lee DPS, Fam J, Kim JE. The impact of 5-hydroxytryptophan supplementation on sleep quality and gut microbiota composition in older adults: A randomized controlled trial. *Clin Nutr.* 2024;43(3):593-602. doi:10.1016/j.clnu.2024.01.010.
- [3] Byun JI, Shin YY, Chung SE, Shin WC. Safety and Efficacy of Gamma-Aminobutyric Acid from Fermented Rice Germ in Patients with Insomnia Symptoms: A Randomized, Double-Blind Trial. *J Clin Neurol.* 2018;14(3):291-295. doi:10.3988/jcn.2018.14.3.291.
- [4] Yamatsu A, Yamashita Y, Pandharipande T, Maru I, Kim M. Effect of oral gamma-aminobutyric acid (GABA) administration on sleep and its absorption in humans. *Food Sci Biotechnol.* 2016;25 (2): 547-551. doi:10.1007/s10068-016-0076-9.
- [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] Moulin M, Crowley DC, Guthrie N, Lewis ED, Xiong L. Safety and Efficacy of AlphaWave L-Theanine Supplementation for 28 Days in Healthy Adults with Moderate Stress: A Randomized, Double-Blind, Placebo-Controlled Trial. *Neurol Ther.* 2024;13(4):1135-1153. doi:10.1007/s40120-024-00624-7.
- [7] Lyon MR, Kapoor MP, Juneja LR. The effects of L-theanine (Suntheanine) on objective sleep quality in boys with attention deficit hyperactivity disorder (ADHD): a randomized, double-blind, placebo-controlled clinical trial. *Altern Med Rev.* 2011;16(4):348-354.
- [8] University Hospital Zurich. Sleep medicine consultation, Department of Pulmonology, Sleep laboratory, West C 11, Raemistrasse 100, 8091 Zurich, Switzerland.
- [9] University Hospital Zurich. Interdisciplinary center for sleep disorders. Clinical Neuroscience Center, University Hospital Zurich.