

# NVTIA Tomato-Derived Phytomelatonin Produced by Combined Enzymatic Hydrolysis and Extraction: Process Rationale, Stability-Oriented Design, and Translational Evidence

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## ABSTRACT

We evaluated the NVTIA tomato-derived phytomelatonin process as a differentiated natural ingredient platform in the context of contemporary literature on phytomelatonin, tomato biology, melatonin stability, and translational sleep-health evidence. Using the available process-associated dataset, we summarized three optimized production examples and three comparator conditions and then contextualized these findings with peer-reviewed publications on phytomelatonin occurrence in edible plants, tomato melatonin biosynthesis, process-sensitive melatonin degradation, black ginger bioactivity, polyamine biology, and clinical melatonin literature. Across the optimized examples, melatonin content ranged from 98.2% to 99.1%, impurity content remained at or below 1.5%, and microbial limits were reported as compliant. In contrast, comparator conditions without rice germ polyamines or with off-window pH or temperature produced markedly lower melatonin content (82.3%-85.5%) and higher impurity burdens (8.2%-10.5%). Published literature supports the plausibility of a tomato-centered phytomelatonin strategy because tomatoes are recognized edible sources of phytomelatonin and their melatonin biosynthetic route has been mechanistically characterized. The same literature also shows that pH, temperature, light, and storage conditions materially affect melatonin stability, which gives process meaning to the NVTIA emphasis on mild enzymolysis, chromatographic purification, and stabilization. Black ginger and rice germ polyamines provide an additional mechanistic basis for antioxidant and cell-protective positioning, although their direct contribution to finished-product clinical efficacy remains inferential rather than proven. Taken together, the evidence supports NVTIA as a tomato-derived phytomelatonin ingredient with a stability-oriented process design and favorable analytical profile. However, any explicit superiority claim over equivalent commercial materials still requires independent head-to-head analytics, batch reproducibility studies, and controlled human trials.

## KEYWORDS

Phytomelatonin; Tomato-derived melatonin; Enzymatic hydrolysis; NVTIA; Black ginger; Rice germ polyamines; Stability; Sleep support

## 1. INTRODUCTION

Melatonin is an indoleamine with established relevance to circadian regulation and broad redox biology, and interest in naturally sourced melatonin has expanded as the nutraceutical sector has moved toward food-derived actives and cleaner process narratives [1, 10, 11]. We therefore asked whether a tomato-centered phytomelatonin platform could achieve scientifically differentiated value on the basis of source biology, process control, analytical purity, and storage stability.

Tomatoes are repeatedly identified as edible plant sources of phytemelatonin, yet the literature also makes clear that melatonin content is variable across tissues, developmental stages, environmental conditions, and analytical methods [1-3]. This variability creates a familiar industrial challenge: a natural source may be attractive from a market perspective, but the process must still solve for release efficiency, analytical purity, impurity control, and storage stability.

A tomato-centered phytemelatonin platform may be differentiated not only by its natural-source origin but also by a process architecture that improves release efficiency, purity control, and storage stability. In the present study, process-associated analytical results were interpreted together with peer-reviewed evidence on phytemelatonin biology, tomato biochemistry, co-matrix functionality, and translational melatonin science.

## **2. STUDY DESIGN AND ANALYTICAL BASIS**

The analytical basis of the study comprised three optimized process runs and three comparator conditions, with finished-product melatonin content, impurity burden, and microbial compliance as the primary endpoints. These findings were interpreted alongside literature on phytemelatonin distribution in edible plants, tomato melatonin biosynthesis, postharvest tomato physiology, black ginger bioactivity, polyamine-mediated cytoprotection, and clinical melatonin outcomes [1-11].

Together, the analytical dataset and external literature establish a rigorous biochemical and translational context for discussing the NVTIA platform while maintaining a clear distinction between process-associated performance and clinically demonstrated efficacy.

## **3. PROCESS RATIONALE FOR THE NVTIA PLATFORM**

The NVTIA process centers on tomato raw material as the principal phytemelatonin source and combines that matrix with Thai black ginger and rice germ polyamines. The process window disclosed for enzymolysis uses pectinase, cellulase, and a compound enzyme preparation at pH 4.0-6.0 and 40-60 °C, followed by solvent extraction, gel-chromatographic purification, stabilization, membrane filtration, and vacuum drying.

From a process-engineering perspective, this architecture is distinctive for four reasons. First, it directly addresses the structural barrier imposed by tomato cell-wall polysaccharides, especially pectin and cellulose, that may limit release of intracellular melatonin. Second, it uses mild enzymatic conditions instead of relying only on aggressive extraction. Third, it inserts a purification and stabilization sequence rather than treating extraction yield as the only endpoint. Fourth, it frames black ginger and rice germ polyamines as functional co-matrix components rather than incidental additives.

The scientific plausibility of a tomato-based strategy is reinforced by plant and tomato literature. Reviews of phytemelatonin identify tomato as a meaningful edible source [1, 2], and mechanistic work in tomato has clarified the biosynthetic pathway and demonstrated that melatonin accumulation can be biologically regulated within the fruit [3]. Independent tomato studies also show that melatonin influences postharvest ripening and metabolite profiles, further supporting tomato as a biologically relevant matrix rather than a random source material [4, 5].

## **4. PROCESS-ASSOCIATED ANALYTICAL PERFORMANCE**

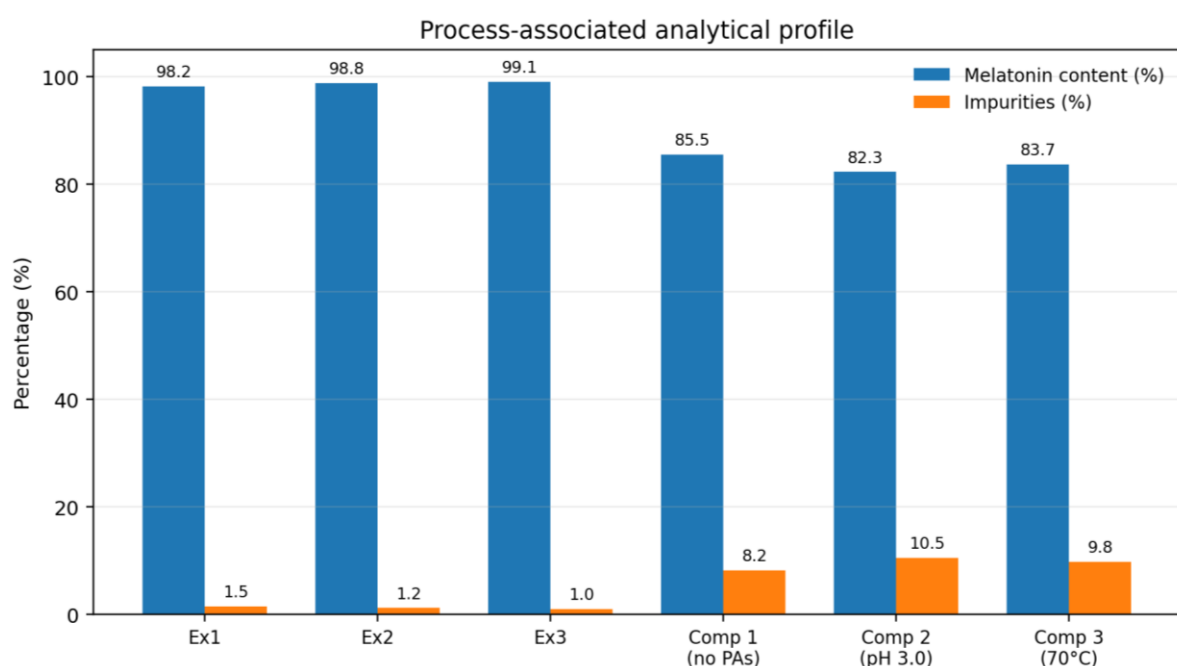
The available analytical dataset is summarized in Table 1 and Figure 1. The optimized examples produced finished products with melatonin content of 98.2%, 98.8%, and 99.1%, while impurity levels were controlled at 1.5%, 1.2%, and 1.0%, respectively. In all three optimized runs, microbial limits were reported as compliant.

The comparator runs identify the most consequential process sensitivities. Removing rice germ polyamines reduced melatonin content to 85.5% and increased impurities to 8.2%. Shifting the enzymatic-hydrolysis pH to 3.0 reduced melatonin content to 82.3% and increased impurities to 10.5%. Raising the enzymatic-hydrolysis temperature to 70 °C reduced melatonin content to 83.7% and increased impurities to 9.8%.

Viewed together, these patterns suggest that the NVTIA platform is not merely a tomato extract with a melatonin claim. Rather, the process performance appears to depend on a coordinated window in which matrix disassembly, melatonin preservation, and downstream polishing are balanced. The available data therefore support a differentiation claim at the level of process logic and analytical profile, even though they do not yet prove superiority against external commercial benchmarks.

**Table 1.** Process-associated analytical outcomes under optimized and comparator conditions

Group	Melatonin (%)	Impurities (%)	Microbial limits
Example 1	98.2	≤1.5	Complies
Example 2	98.8	≤1.2	Complies
Example 3	99.1	≤1.0	Complies
Comparator 1 (no rice germ polyamines)	85.5	8.2	Complies
Comparator 2 (pH = 3.0)	82.3	10.5	Complies
Comparator 3 (70°C)	83.7	9.8	Complies



**Figure 1.** Optimized runs maintained high melatonin content and low impurity burden, whereas comparator conditions showed marked deterioration

## 5. LITERATURE CONTEXT AND BIOLOGICAL INTERPRETATION

The literature strongly supports the phytomelatonin premise while also showing that reported concentrations vary substantially across studies and analytical platforms [1, 2]. For ingredient development, this means that source selection alone is insufficient and that process control is central to product quality.

Tomato-specific research adds mechanistic depth. Zhang and colleagues elucidated key biosynthetic genes and showed that melatonin enrichment in tomato fruit is biologically tractable [3]. Sun et al.

reported that exogenous melatonin promotes ripening and improves quality-related features during tomato postharvest life [4], and Dou et al. further showed that melatonin can shape accumulation of primary and secondary metabolites in tomato fruit [5]. These studies do not validate the NVTIA ingredient directly, but they strengthen the argument that a tomato-based phytomelatonin ingredient is biologically coherent.

Stability is another major differentiator. Prnil et al. showed that melatonin degradation is materially affected by pH, temperature, light, and storage conditions, with lower-pH conditions and lower thermal stress generally favoring stability [9]. This finding is highly relevant to the NVTIA technical logic because it explains why mild enzymatic-hydrolysis windows, solvent removal, chromatographic purification, and an explicit stabilization step may matter as much as the extraction step itself.

The supporting co-matrix components are also scientifically interpretable, but only within limits. Black ginger (*Kaempferia parviflora*) is rich in methoxyflavones and has a literature base consistent with antioxidant and broader bioactive potential [6]. Polyamines such as spermidine, spermine, and putrescine are linked to cytoprotection, autophagy-related biology, and stress adaptation in diverse systems [7, 8]. However, the literature does not yet prove that combining black ginger and rice germ polyamines with tomato-derived phytomelatonin necessarily yields superior human outcomes. What it does provide is a credible mechanistic rationale for why such a formulation might deserve deeper testing.

**Table 2.** Literature-supported scientific rationale for the NVTIA platform

Platform element	Scientific rationale	Representative source(s)
Tomato as core matrix	Edible source of phytomelatonin with documented occurrence and a characterized biosynthetic pathway	[1]-[3]
Mild enzymolysis window	Targets pectin- and cellulose-rich barriers while avoiding excessive thermal stress	[3], [9]
Purification and stabilization	Analytically relevant because melatonin is sensitive to pH, temperature, light, and storage conditions	[9]
Black ginger inclusion	Provides an antioxidant/bioactive rationale through methoxyflavone-rich phytochemistry	[6]
Rice germ polyamines	Adds a cell-protective and stress-adaptation rationale via spermidine/spermine biology	[7], [8]
Sleep-support relevance	Aligned with broader clinical melatonin evidence, though not yet specific to this ingredient	[10], [11]

## 6. TRANSLATIONAL RELEVANCE AND CLINICAL CORRELATION

Clinical melatonin literature further supports the translational relevance of this ingredient class. A systematic review and meta-analysis of randomized controlled trials found that melatonin supplementation overall improved sleep quality, although effects were not uniform across all populations and study designs [10]. A broader clinical review similarly concluded that melatonin has meaningful physiological relevance, while emphasizing dose, population, formulation, and long-term use considerations [11].

These clinical data support the general proposition that melatonin-containing ingredients are relevant to sleep-related applications, but they do not automatically transfer to every phytomelatonin ingredient. NVTIA is therefore best characterized as a biologically aligned natural-source platform with a favorable analytical profile. Definitive claims regarding superior efficacy, onset, durability, or tolerability compared with equal-dose alternatives still require controlled trials using the finished NVTIA material.

## 7. DISCUSSION

We interpret the current evidence to mean that NVTIA can reasonably be described as a differentiated phytomelatonin platform for three main reasons. First, the source narrative is commercially and scientifically relevant: tomato is a documented edible source of phytomelatonin rather than a synthetic conversion intermediate [1-3]. Second, the process narrative is unusually coherent: cell-wall-targeted enzymolysis, controlled pH and temperature, chromatographic purification, and stabilization together form a stability-oriented manufacturing logic that is consistent with known melatonin chemistry [9]. Third, the available analytical results are directionally strong, with optimized runs approaching 99% melatonin content while comparator conditions deteriorate sharply.

Differentiation should nevertheless be distinguished from proven superiority. The currently available NVTIA dataset supports stronger performance than its own component-deletion and off-window process comparators, but it does not yet establish superiority over other commercial phytomelatonin ingredients, synthetic melatonin products, or tomato-derived materials produced by alternative methods.

Further validation should therefore include batch-to-batch reproducibility studies, orthogonal purity confirmation by validated LC-MS/MS or equivalent analytical methods, stress stability testing under commercial storage conditions, and randomized human studies performed with a fully characterized finished NVTIA ingredient.

## 8. FUTURE DIRECTIONS

Future work should focus on linking the observed analytical advantages to product-level performance. Particularly important priorities include quantitative stability modeling, impurity-speciation profiling, bioaccessibility and pharmacokinetic comparison with reference materials, and head-to-head human studies evaluating sleep-related outcomes, tolerability, and formulation robustness.

## 9. CONCLUSION

In conclusion, the NVTIA tomato-derived phytomelatonin process demonstrates a credible scientific basis for differentiation as a natural-source ingredient platform. Its coordinated enzymatic hydrolysis window, purification strategy, and stabilization sequence are consistent with literature-supported determinants of melatonin release, preservation, and analytical quality. Within the currently available dataset, optimized conditions yielded high melatonin content, low impurity burden, and compliant microbiological outcomes, whereas comparator conditions showed clear deterioration in performance.

Overall, NVTIA is best characterized as a tomato-derived phytomelatonin platform with a stability-oriented design, coherent process logic, and credible translational relevance. Additional direct comparative and clinical studies will determine the extent to which these analytical advantages translate into product superiority in practical use.

## REFERENCES

- [1] Arnao, M. B., & Hernández-Ruiz, J. (2018). The potential of phytomelatonin as a nutraceutical. *Molecules*, 23(1), 238. <https://doi.org/10.3390/molecules23010238>
- [2] Murch, S. J., & Erland, L. A. E. (2021). A systematic review of melatonin in plants: An example of evolution of literature. *Frontiers in Plant Science*, 12, 683047. <https://doi.org/10.3389/fpls.2021.683047>
- [3] Zhang, Z., Zhang, X., Chen, Y., et al. (2023). Understanding the mechanism of red light-induced melatonin biosynthesis facilitates the engineering of melatonin-enriched tomatoes. *Nature Communications*, 14, 5525. <https://doi.org/10.1038/s41467-023-41307-5>

- [4] Sun, Q., Zhang, N., Wang, J., et al. (2015). Melatonin promotes ripening and improves quality of tomato fruit during postharvest life. *Journal of Experimental Botany*, 66(3), 657–668. <https://doi.org/10.1093/jxb/eru332>
- [5] Dou, J., Wang, J., Tang, Z., et al. (2022). Application of exogenous melatonin improves tomato fruit quality by promoting the accumulation of primary and secondary metabolites. *Foods*, 11(24), 4097. <https://doi.org/10.3390/foods11244097>
- [6] Elshamy, A. I., Mohamed, T. A., Essa, A. F., et al. (2019). Recent advances in *Kaempferia* phytochemistry and biological activity: A comprehensive review. *Nutrients*, 11(10), 2396. <https://doi.org/10.3390/nu11102396>
- [7] Ni, Y. Q., & Liu, Y. S. (2021). New insights into the roles and mechanisms of spermidine in aging and age-related diseases. *Aging and Disease*, 12(8), 1948–1963. <https://doi.org/10.14336/AD.2021.0603>
- [8] Madeo, F., Carmona-Gutierrez, D., Kepp, O., & Kroemer, G. (2019). Spermidine: a physiological autophagy inducer acting as an anti-aging vitamin in humans? *Autophagy*, 15(1), 165–168. <https://doi.org/10.1080/15548627.2018.1530929>
- [9] Prani, T., Moonngarm, A., & Loypimai, P. (2020). Influence of pH, temperature, and light on the stability of melatonin in aqueous solutions and fruit juices. *Heliyon*, 6(3), e03648. <https://doi.org/10.1016/j.heliyon.2020.e03648>
- [10] Fatemeh, G., Sajjad, M., Niloufar, R., et al. (2022). Effect of melatonin supplementation on sleep quality: a systematic review and meta-analysis of randomized controlled trials. *Journal of Neurology*, 269, 205–216. <https://doi.org/10.1007/s00415-020-10381-w>
- [11] Givler, D., Givler, A., Luther, P. M., et al. (2023). Chronic administration of melatonin: Physiological and clinical considerations. *Neurology International*, 15(1), 518–533. <https://doi.org/10.3390/neurolint15010031>