

NVTIA GABA-Lysine Calcium Composite Microsphere System for Promoting Calcium Absorption: Formulation Architecture, Gastrointestinal Dispersion, and Bone-Support Evidence

Jabar Yassine *, Zoey Parker, Gregg L. Semenza

World Food Supplement Association, New York, USA

*Corresponding Author: info@wfsas.org

ABSTRACT

We present an NVTIA composite microsphere system that combines a phosphorylated algal-calcium core, a GABA-L-lysine inclusion complex, a natto-derived MK-7 and Agaricus bisporus-derived vitamin D2 deposition module, and vitamin E protection. We analyzed the formulation-specific comparative dataset together with published human and translational evidence relevant to calcium absorption and skeletal utilization. In the comparative preparation, the integrated microsphere system dispersed completely in simulated intestinal fluid within 2 min, whereas the conventional comparator remained incompletely dispersed beyond 8 min. Core active retention reached at least 99.0% for GABA/L-lysine and at least 98.8% for MK-7/vitamin D2, and 30-day room-temperature retention remained at least 97.5%, compared with 82.3%, 86.7%, and 78.5%, respectively, in the comparator. Published studies aligned with the formulation modules: L-lysine significantly increased intestinal calcium absorption in 45 osteoporotic patients [2]; CPP enhanced skeletal 45Ca incorporation in growing rats [4]; algal calcium achieved a fractional absorption of 23.1 +/- 6.4% versus 14.7 +/- 6.4% for CaCO₃ in postmenopausal women [5]; UV-B-irradiated button-mushroom vitamin D2 raised serum vitamin D indices similarly to supplemental vitamin D2 [7]; and recent meta-analytic evidence indicates that vitamin K, especially K2, primarily improves osteocalcin carboxylation and may help preserve lumbar-spine bone density [9]. We interpret these converging data as support for a coordinated calcium-delivery architecture that merits further bioavailability and outcome-based validation.

KEYWORDS

NVTIA; Calcium absorption; Algal calcium; L-lysine; GABA; Casein phosphopeptide; Vitamin K2 MK-7; Vitamin D2; Composite microsphere

1. INTRODUCTION

Calcium supplementation is biologically meaningful only when the mineral is released, solubilized, transported, and subsequently incorporated into bone-related metabolic pathways with adequate efficiency. We therefore approach the NVTIA platform as a coordinated delivery architecture rather than a simple calcium-plus-vitamin blend. Intestinal calcium uptake proceeds through both transcellular and paracellular mechanisms, with vitamin D-dependent regulation remaining central to the active transport pathway [1]. This physiological framework helps explain why formulation-level design can materially influence practical performance.

In the present manuscript, we focus on four linked modules: a phosphorylated algal-calcium microsphere core intended to stabilize the calcium source; an absorption-support complex built from GABA, L-lysine, CPP, and carboxymethyl-beta-cyclodextrin; a deposition-oriented micronutrient

module containing natto-derived MK-7 and mushroom-derived vitamin D2; and an antioxidant-protective shell based on vitamin E. Instead of treating these elements as isolated ingredients, we interpret them as a staged system that addresses dissolution, contact with absorptive pathways, and post-absorption skeletal utilization in sequence.

Our objective is to present a publication-ready manuscript that retains the formulation-specific comparative dataset while anchoring the major design choices to peer-reviewed evidence. This structure allows the formulation data and the external literature to speak to the same biological question: how a multi-module calcium system may improve absorption-linked and bone-supportive performance relative to conventional compounded preparations.

2. MATERIALS AND METHODS

2.1. Formulation Architecture

We organized the NVTIA composition into four functional modules and summarized the composition window shown in the formulation dataset (Table 1). The overall formulation architecture is illustrated in Figure 1.

Table 1. Functional modules and composition window of the NVTIA composite microsphere system

Module	Parts by weight	Main disclosed constituents
Calcium-source modified microsphere	60-80	Algal calcium + dicalcium phosphate + chitosan + phosphorylation reagent
Absorption-promoting inclusion component	15-25	GABA, L-lysine, CPP, carboxymethyl-beta-cyclodextrin
Calcium-directed deposition component	3-8	Natto-derived K2 MK-7 + Agaricus bisporus-derived vitamin D2
Synergistic enhancement component	0.05-0.15	Natural vitamin E

Formulation architecture summarised from the patent disclosure



Figure 1. Formulation architecture of the NVTIA composite microsphere system

2.2. Comparative Framework And Readouts

For the formulation-specific comparison, we used the integrated composite microsphere (Example 2) and the conventional compounded preparation described in the dataset. Their structural and compositional differences are summarized in Table 2, and the principal performance readouts are summarized in Table 3. The overall comparative formulation performance is illustrated in Figure 2.

Table 2. Structural and compositional comparison between NVTIA Example 2 and the comparative formulation.

Indicator	NVTIA Example 2	Comparative formulation
Calcium-source core	Phosphorylated algal calcium + dicalcium phosphate + chitosan microsphere	Calcium carbonate + dicalcium phosphate direct mix
Absorption-support module	GABA + L-lysine + CPP + carboxymethyl-beta-cyclodextrin inclusion complex	CPP + vitamin C direct blend
Deposition module	Natto-derived K2 MK-7 + Agaricus bisporus-derived vitamin D2	Same K2 MK-7 and vitamin D2 module
Assembly mode	Adsorption assembly + spray-dried integrated composite microsphere	Conventional compounded preparation

Table 3. Performance comparison between NVTIA Example 2 and the comparative formulation

Performance readout	NVTIA Example 2	Comparative formulation
Dispersion in simulated intestinal fluid	Complete within 2 min	Not complete within 8 min
Core active retention	GABA/L-lysine $\geq 99.0\%$; K2 MK-7/VD2 $\geq 98.8\%$	Conventional actives 82.3%; K2 MK-7/VD2 86.7%
30-day room-temperature retention	$\geq 97.5\%$	78.5%
Structural behaviour	Orderly swelling and staged release	Irregular swelling; overly fast release
Centrifugation binding test	No stratification, precipitation or dissociation	Slight stratification and precipitation

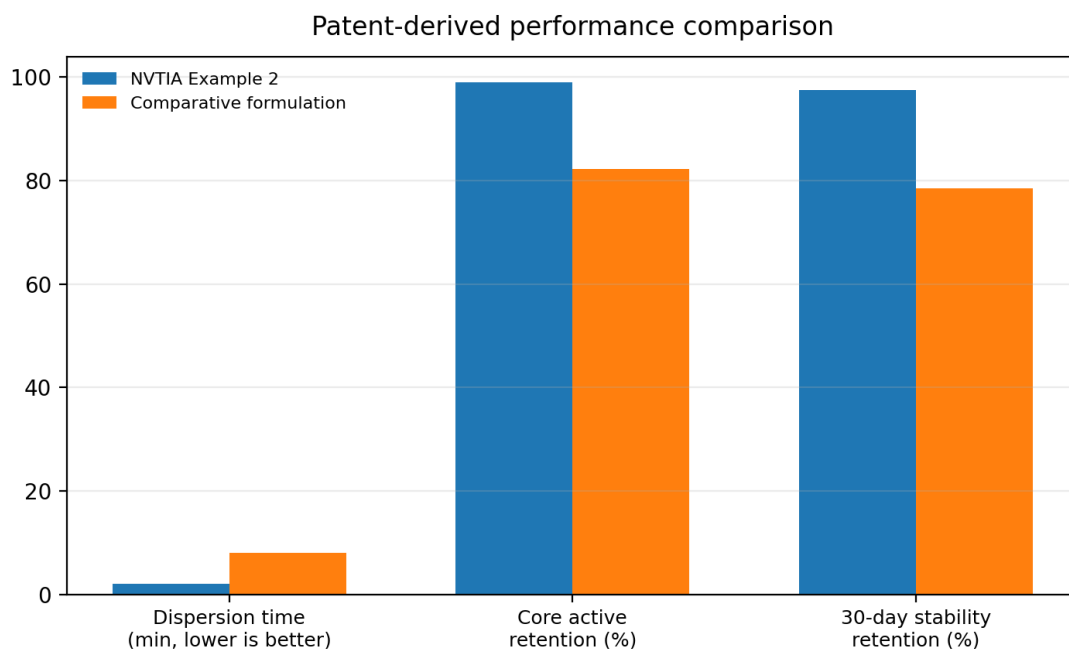


Figure 2. Comparative formulation performance based on the formulation dataset

2.3. Published Evidence Retrieval And Alignment

We then matched the formulation modules to published studies on calcium transport, lysine-associated absorption, CPP-mediated calcium bioavailability, algal-calcium absorption, mushroom-derived vitamin D2 bioavailability, vitamin K2-related bone metabolism, and GABA-linked osteogenesis [1-10]. Our purpose was not to replace the formulation dataset with unrelated literature, but to evaluate whether the system-level design is biologically coherent when viewed against existing human and translational evidence.

3. RESULTS

3.1. Coordinated Architecture of the Calcium-Delivery System

The NVTIA platform differs from the comparator at the architectural level. The calcium source is not presented as a simple direct blend; rather, it is reorganized into a phosphorylated algal-calcium microsphere, then associated with an inclusion complex containing GABA, L-lysine, CPP, and cyclodextrin chemistry. This layered design is important because the comparator retains the same broad goal - oral calcium supplementation - but lacks both the modified microsphere core and the dedicated GABA-L-lysine inclusion strategy.

We interpret the role of each module as sequential. The core is expected to stabilize the mineral source, the inclusion complex to improve contact with absorption-relevant molecules, the MK-7 and vitamin D2 module to support downstream skeletal utilization, and vitamin E to protect the integrated structure during processing and storage. On this reading, NVTIA is best understood as a delivery system with staged functional logic rather than a loose multi-ingredient mixture.

3.2. Dispersion, Retention, And Short-Term Stability

The formulation dataset shows a consistent performance advantage for the integrated microsphere. In simulated intestinal fluid, Example 2 dispersed completely within 2 min, whereas the comparator did not disperse completely within 8 min. Retention of the GABA/L-lysine module reached at least 99.0% in Example 2, and retention of MK-7/vitamin D2 reached at least 98.8%; the comparator retained 82.3% of its conventional absorption-support actives and 86.7% of MK-7/vitamin D2. Thirty-day room-temperature retention was likewise higher in Example 2 (at least 97.5%) than in the comparator (78.5%).

We also note qualitative differences in structural behavior. Example 2 displayed orderly swelling and staged release without stratification or dissociation under centrifugation, while the comparator showed irregular swelling with slight stratification and precipitation. These findings support a formulation-performance interpretation in which microsphere organization and inclusion chemistry materially improve handling robustness and active preservation.

3.3. Alignment with Published Human And Translational Evidence

The published literature strengthens the biological plausibility of the formulation modules summarized above. The major human and translational studies aligned with the NVTIA system are summarized in Table 4. L-lysine has already been shown in humans to increase intestinal calcium absorption and renal conservation of absorbed calcium [2]. CPP is supported by both a recent review of its calcium-bioavailability properties [3] and an animal study showing significantly higher skeletal ⁴⁵Ca incorporation when CPP is added to calcium-fortified milk [4]. The algal-calcium core is also consistent with human isotope data showing markedly higher fractional absorption than calcium carbonate in postmenopausal women [5].

The post-absorption module is similarly supported. In healthy adults, UV-B-irradiated button mushroom vitamin D2 increased serum vitamin D indices in a manner comparable to supplemental vitamin D2 [7], and a later randomized study showed a 128% increase in serum 25(OH)D2 after four weeks of vitamin D2-enhanced mushroom intake [8]. For vitamin K, a recent meta-analysis indicates that the most reproducible effect is improved osteocalcin carboxylation, with secondary benefit on lumbar-spine bone density in middle-aged and older adults [9]. Although GABA is less established as a calcium supplement ingredient, emerging mechanistic evidence shows that it can stimulate osteoblast differentiation and mineralization, which supports its inclusion as part of a broader bone-support architecture [10].

Table 4. Published evidence supporting the functional modules of the NVTIA system

Published study	Model / sample	Key result	Relevance to NVTIA system
Civitelli et al., 1992 [2]	45 osteoporotic patients; 800 mg/day amino-acid supplementation	L-lysine significantly increased intestinal ⁴⁷ Ca absorption and improved renal conservation of absorbed calcium.	Supports the lysine-containing absorption module.
Tsuchita et al., 2001 [4]	Growing rats; Ca-fortified milk +/- CPP	Extrinsic CPP increased femur and tibia ⁴⁵ Ca incorporation versus control (P < 0.05).	Supports CPP-mediated calcium bioavailability.
Uenishi et al., 2010 [5]	10 postmenopausal women; dual stable isotopes	Fractional absorption of algal calcium was 23.1 ± 6.4% vs 14.7 ± 6.4% for CaCO ₃ (p = 0.006).	Supports the algal-calcium core strategy.
Shankar et al., 2018 [6]	24 osteopenia patients randomized to three calcium preparations	Relative oral bioavailability of calcium lysinate was 223.15%; BMD T-score improvement was strongest in the calcium lysinate group.	Supports amino-acid-assisted calcium delivery.
Urbain et al., 2011 [7]	Vitamin D-deficient adults, randomized trial	UV-B-irradiated button mushroom vitamin D2 increased serum 25OHD similarly to supplemental vitamin D2.	Supports mushroom-derived vitamin D2 as a bioavailable deposition module.
Stepien et al., 2013 [8]	90 adults, 4-week randomized study	Vitamin D2-enhanced mushrooms increased serum 25(OH)D2 by 128% from baseline.	Supports food-form vitamin D2 delivery.
Xie et al., 2024 [9]	Meta-analysis of randomized trials	Vitamin K, especially K2, mainly improved osteocalcin carboxylation and helped maintain/increase lumbar spine BMD.	Supports inclusion of MK-7 in post-absorption bone utilization.
Karunaratne et al., 2023 [10]	MC3T3-E1 cells and zebrafish larvae	GABA stimulated osteoblast differentiation/mineralization and improved vertebral formation.	Provides mechanistic support for including GABA beyond simple excipient logic.

4. DISCUSSION

We regard the main strength of the NVTIA platform as architectural coherence. The formulation-specific comparison alone indicates better dispersion, better active retention, and better short-term stability than the conventional comparator. Those findings would still be limited if they lacked biological context. However, the external literature shows that the chosen modules are not arbitrary: lysine is linked to calcium absorption, CPP is linked to calcium bioavailability, algal calcium can show favorable human absorption, mushroom vitamin D2 is bioavailable, and MK-7 has a plausible role in calcium utilization through osteocalcin carboxylation [2-9].

This alignment does not by itself establish clinical superiority in fracture prevention or long-term bone outcomes. The current evidence base remains a hybrid of formulation-specific comparative data and separate published studies, not a single randomized trial of the full NVTIA system. Even so, the convergence of rapid dispersion, strong active retention, and module-consistent literature support suggests that the formulation is positioned more credibly as a calcium-absorption and bone-support system than a conventional direct-blend product.

We therefore think the most defensible publication posture is a formulation-engineering manuscript with translational interpretation. Future work should prioritize direct bioavailability studies of the complete microsphere, followed by controlled human trials using fractional calcium absorption, serum vitamin D indices, osteocalcin carboxylation markers, and bone-density outcomes as linked endpoints.

5. CONCLUSIONS

We conclude that the NVTIA GABA-Lysine Calcium Composite Microsphere System represents a coordinated oral calcium-delivery architecture in which mineral-source engineering, inclusion-based absorption support, and post-absorption deposition support are assembled into one platform. In the formulation dataset, this design dispersed faster, retained actives more effectively, and remained more stable than the comparator. When those formulation data are interpreted alongside published evidence on lysine, CPP, algal calcium, MK-7, mushroom-derived vitamin D2, and GABA-related osteogenesis, the overall system shows a coherent rationale for improved calcium-absorption performance and bone-support potential.

REFERENCES

- [1] Bronner F. Mechanisms of intestinal calcium absorption. *J Cell Biochem.* 2003; 88(2):387-393. doi:10.1002/jcb.10330.
- [2] Civitelli R, Villareal DT, Agnusdei D, Nardi P, Avioli LV, Gennari C. Dietary L-lysine and calcium metabolism in humans. *Nutrition.* 1992; 8(6):400-405. PMID:1486246.
- [3] Liu G, et al. A comprehensive review on preparation, structure-activities relationship, and calcium bioavailability of casein phosphopeptides. *Crit Rev Food Sci Nutr.* 2024; 64(4):996-1014. doi:10.1080/10408398.2022.2111546.
- [4] Tsuchita H, Suzuki T, Kuwata T. The effect of casein phosphopeptides on calcium absorption from calcium -fortified milk in growing rats. *Br J Nutr.* 2001; 85(1):5-10. PMID:11227028.
- [5] Uenishi K, Fujita T, Ishida H, et al. Fractional Absorption of Active Absorbable Algal Calcium (AAACa) and Calcium Carbonate Measured by a Dual Stable-Isotope Method. *Nutrients.* 2010; 2(7):752-761. doi:10.3390/nu2070752.
- [6] Shankar K, Bansal A, Jain A, et al. A Randomized Open-Label Clinical Study Comparing the Efficacy, Safety, and Bioavailability of Calcium Lysinate with Calcium Carbonate and Calcium Citrate Malate in Osteopenia Patients. *J Orthop Case Rep.* 2018; 8(1):15-19. PMID:30687654.
- [7] Urbain P, Singler F, Ihorst G, Biesalski HK, Bertz H. Bioavailability of vitamin D2 from UV-B-irradiated button mushrooms in healthy adults deficient in serum 25-hydroxyvitamin D: a randomized controlled trial. *Eur J Clin Nutr.* 2011; 65(8):965-971. doi:10.1038/ejcn.2011.53.

- [8] Stepien M, O'Mahony L, O'Sullivan A, et al. Effect of supplementation with vitamin D2 -enhanced mushrooms on vitamin D status in healthy adults. *J Nutr Sci.* 2013; 2:e29. doi:10.1017/jns.2013.22.
- [9] Xie C, et al. Effects of vitamin K supplementation on bone mineral density at different sites and bone metabolism in the middle-aged and elderly population: a meta-analysis and systematic review of randomized controlled trials. *Bone Joint Res.* 2024; 13(12):750-763.
- [10] Karunaratne WAHM, Choi YH, Lee MH, Kang CH, Kim GY. Gamma-aminobutyric acid (GABA)-mediated bone formation and its implications for anti-osteoporosis strategies: Exploring the relation between GABA and GABA receptors. *Biochem Pharmacol.* 2023; 218:115888. doi:10.1016/j.bcp.2023.115888.
- [11] NVTIA GABA-Lysine Calcium Supplement Preparation for Promoting Calcium Absorption. Formulation dossier and comparative data file used by the authors.