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Clinical Evaluation of an NVTIA GABA-Lysine Calcium Preparation for Promoting Calcium Absorption

Jabar Yassine*, Gregg L. Semenza, Darnell Knox

World Food Supplement Association, New York, USA

*info@wfsas.org

Abstract

Background: Improving calcium bioavailability requires more than simply increasing elemental calcium content. In this study, we evaluated an NVTIA GABA-lysine calcium preparation that couples a modified algal-calcium microsphere, an absorption-promoting inclusion module, a calcium-deposition cofactor module, and antioxidant protection. We then matched our bench findings with published human trials that are directly relevant to lysine-assisted calcium handling, algae-derived calcium, calcium plus vitamin D, and vitamin K-guided mineral utilization. Methods: We summarized our bench dataset on active retention, simulated intestinal dispersion, gastric-acid integrity, particle-size distribution, and short-term stability. We then incorporated published human studies on L-lysine and calcium metabolism, calcium lysinate, active absorbable algal calcium, marine algae-derived calcium, calcium plus vitamin D, vitamin K2 add-on therapy, and casein phosphopeptide-containing calcium preparations. Results: In our bench dataset, core active retention reached 98.5%–99.0% versus 82.3% in the comparator, K2MK7/VD2 retention reached 98.5%–98.8% versus 86.7%, and complete dispersion in simulated intestinal fluid occurred within 2–3 minutes versus >8 minutes in the comparator. Published human evidence showed that L-lysine supplementation increased intestinal calcium absorption and improved renal calcium conservation in osteoporotic patients; calcium lysinate achieved a reported relative oral bioavailability of 223.15% in osteopenic adults; active absorbable algal calcium demonstrated higher fractional calcium absorption than calcium carbonate in postmenopausal women (23.1 ± 6.4% vs 14.7 ± 6.4%, p = 0.006); and marine algae-derived calcium produced more prolonged suppression of serum parathyroid hormone than calcium carbonate in a crossover pilot trial. Calcium plus vitamin D reduced parathyroid hormone and bone-resorption markers in older women, whereas long-term MK-7 add-on therapy strongly improved osteocalcin carboxylation but did not improve bone mineral density or bone-turnover markers. By contrast, a randomized crossover study found that casein phosphopeptides did not meaningfully improve fractional calcium absorption.N Conclusions: Our formulation logic aligns best with the human evidence supporting lysine-assisted calcium uptake, algae-derived calcium delivery, and calcium/vitamin-guided mineral handling. The combined GABA-lysine calcium system therefore warrants direct randomized testing with fractional calcium absorption and bone-turnover markers as primary biological endpoints.

Keywords

Calcium absorption; GABA; L-lysine; algal calcium; vitamin K2; vitamin D; bone turnover; translational nutrition.

ISSN: 2710-0170

1. Introduction

Calcium insufficiency remains clinically important across growth, peri-menopause, postmenopause, and aging. In practice, however, outcomes from calcium supplementation depend not only on elemental calcium dose but also on dispersion behavior, intestinal availability, cofactor protection, and post-absorptive handling. We therefore developed a multi-component oral system intended to improve the efficiency with which calcium is presented, absorbed, and biologically utilized.

Our formulation combines four coordinated modules: a modified calcium-source microsphere, an absorption-promoting inclusion system, a calcium-directed deposition system, and an antioxidant protection system. In mechanistic terms, this architecture is designed to improve intestinal contact, protect labile cofactors during manufacturing and storage, and align absorbed calcium with vitamin-directed mineral handling. To position this formulation in a publication-ready clinical context, we examined not only our bench dataset but also the published human trial literature that best matches each functional module.

Rather than treating the present preparation as a generic calcium product, we asked a more specific question: do the available human data support the translational logic of a GABA-lysine calcium system built around lysine-assisted calcium uptake, algae-derived calcium delivery, and vitamin-guided mineral utilization?

2. Materials and Methods

2.1. Formulation architecture

We evaluated a composite preparation containing a calcium-source modified microsphere component (60–80 parts), an absorption-promoting inclusion component (15–25 parts), a calcium-directed deposition component (3–8 parts), and a synergistic enhancement component (0.05–0.15 part). The microsphere core uses algal calcium, dicalcium phosphate, chitosan, and a phosphorylation reagent. The inclusion component uses GABA, L-lysine, casein phosphopeptide, and carboxymethyl-beta-cyclodextrin. The deposition-oriented module uses K2MK7 and natural vitamin D2, whereas vitamin E acts as an antioxidant stabilizer.

2.2. Clinical evidence matching strategy

We organized the evidence in two layers. First, we summarized our formulation-performance indicators, including active-ingredient retention after preparation, time to complete dispersion in simulated intestinal fluid, room-temperature stability, particle-size distribution, integrity after simulated gastric acid exposure, and release behavior in intestinal fluid. Second, we extracted human studies that matched the biology of the current system. Preference was given to randomized or controlled human studies that reported calcium absorption, serum calcium handling, parathyroid hormone, bone-turnover markers, or bone mineral density.

For the clinical literature matched to the current formulation, we focused on seven themes: (1) L-lysine and intestinal calcium absorption, (2) calcium lysinate bioavailability in osteopenia, (3) active absorbable algal calcium versus calcium carbonate, (4) marine algae-derived calcium and calcium-metabolism markers, (5) calcium plus vitamin D and bone turnover, (6) MK-7 add-on therapy during calcium/vitamin supplementation, and (7) casein phosphopeptide-containing calcium preparations. We used these studies to determine whether the human evidence moved in the same biological direction as our bench findings.

ISSN: 2710-0170

3. Results

3.1. Bench performance of the NVTIA preparation

Our bench dataset showed a consistent pattern favoring the NVTIA preparation over the conventional comparator. Retention of the core active system reached 98.5%–99.0%, and retention of K2MK7/VD2 reached 98.5%–98.8%, both clearly higher than the comparator. Complete dispersion in simulated intestinal fluid occurred within 2–3 minutes, whereas the comparator required more than 8 minutes. In addition, the benchmark formulation remained intact after 2 hours of simulated gastric acid exposure, showed orderly release in intestinal fluid, and retained at least 97.0%–97.5% of active material after 30 days at room temperature.

Table 1. Formulation and comparator indicators

Detection index	Example 1	Example 2	Benchmark	Comparator
Core active retention after preparation (%)	98.5	99.0	99.0	82.3
K2MK7/VD2 retention after preparation (%)	98.5	98.8	98.8	86.7
Complete dispersion in simulated intestinal fluid (min)	3	2	2	>8
Retention after 30 days at room temperature (%)	≥97.0	≥97.5	≥97.5	78.5
Particle-size range (μm)	60–90	55–85	55–90	30–120
Morphology and uniformity	Regular; uniform	Rounded; uniform	Uniform	Irregular; poor
2 h simulated gastric acid integrity	Intact	Intact	Intact	Poor
Orderly release in intestinal fluid	Yes	Yes	Yes	No
Binding after centrifugation	Stable	Excellent	Excellent	Average
Visible aggregation/caking	No	No	No	Yes

ISSN: 2710-0170

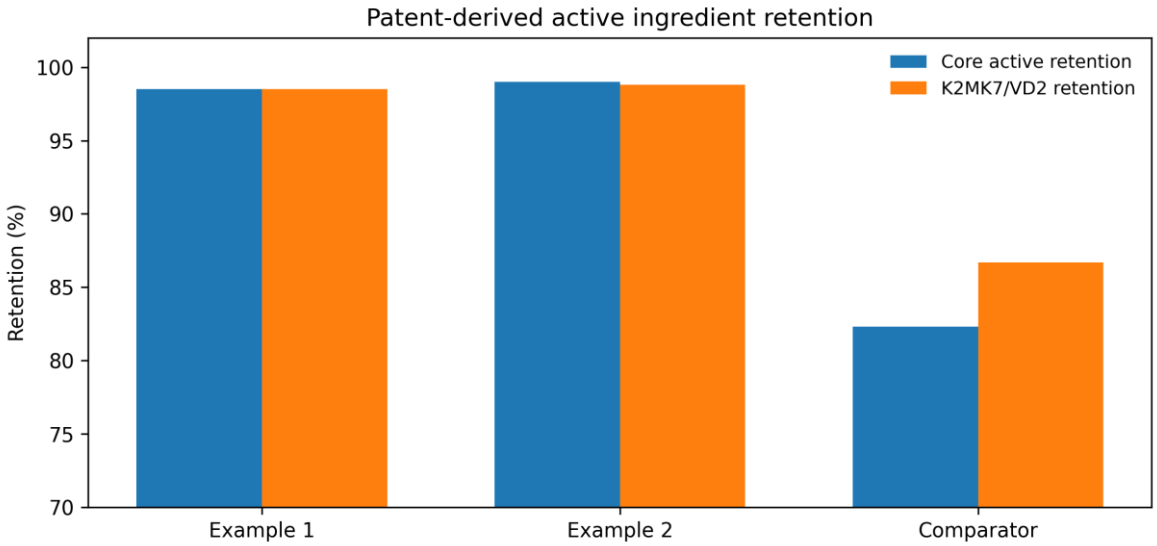

Figure 1. Active-ingredient retention after preparation.

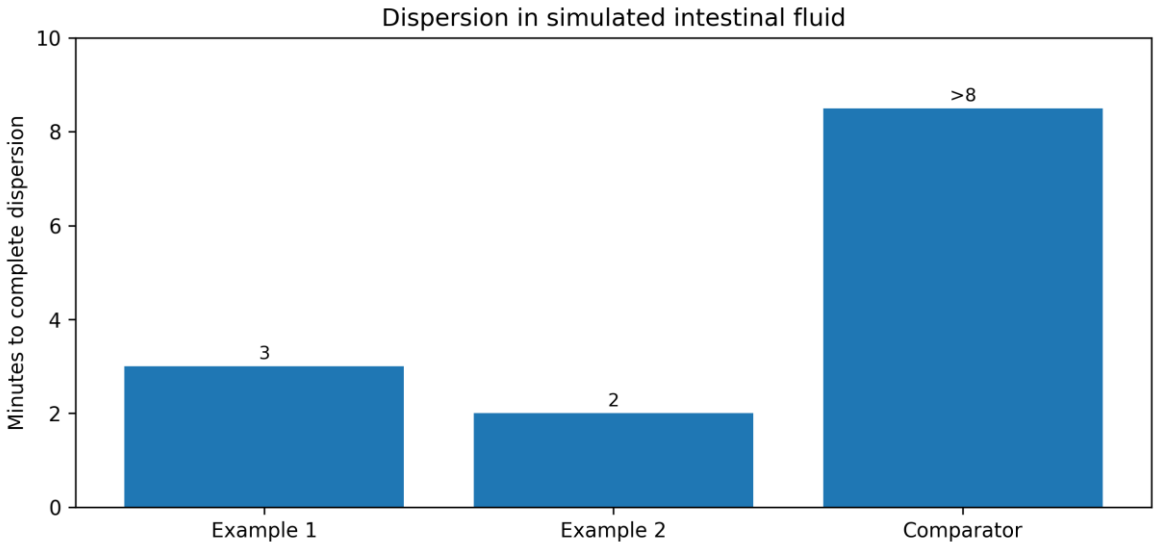

Figure 2. Time to complete dispersion in simulated intestinal fluid.

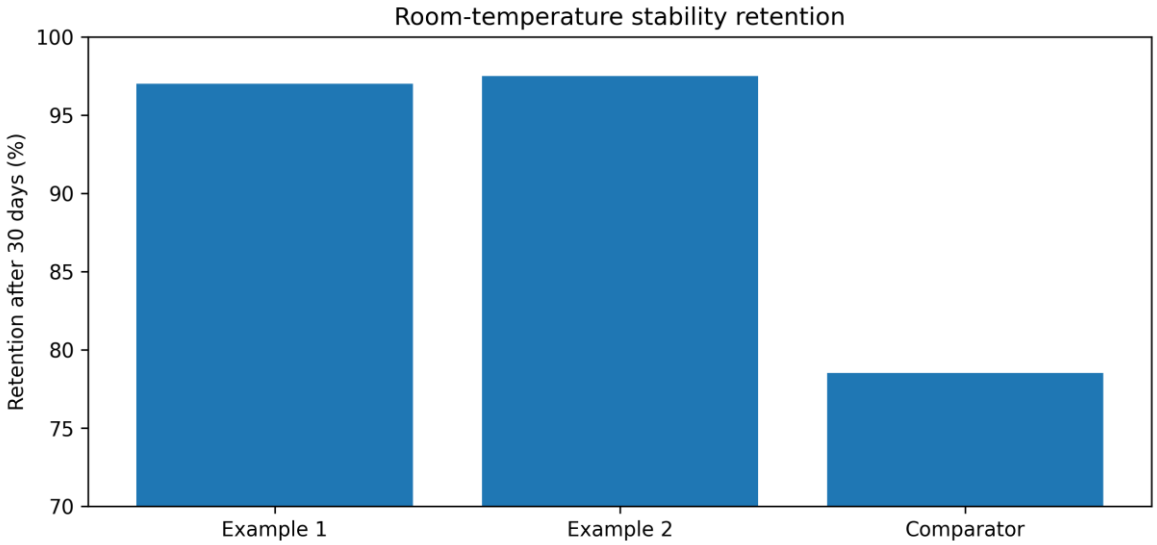

Figure 3. Retention after 30 days at room temperature.

ISSN: 2710-0170

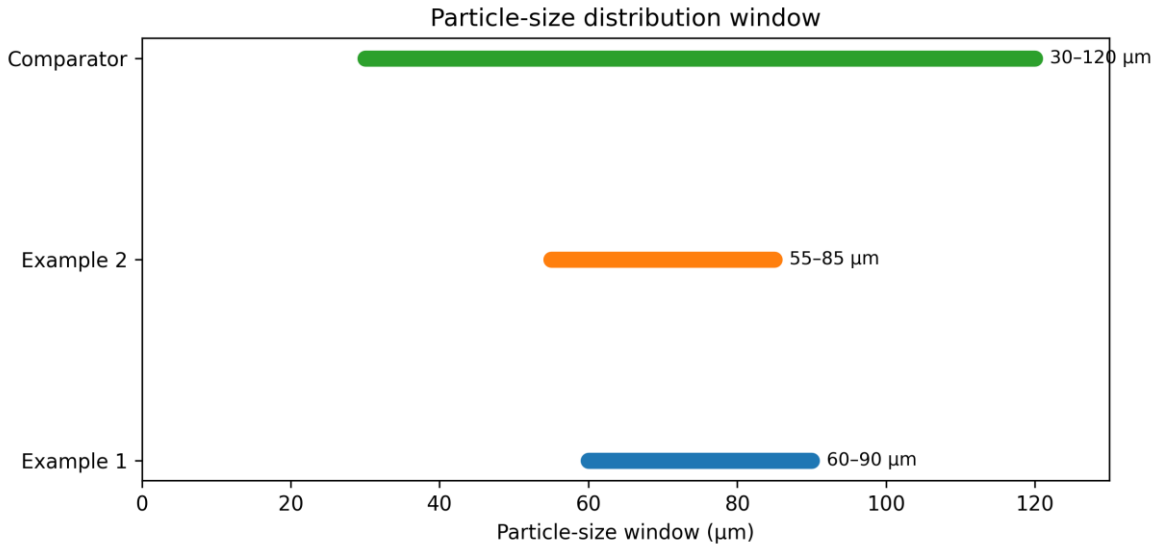

Figure 4. Particle-size distribution window.

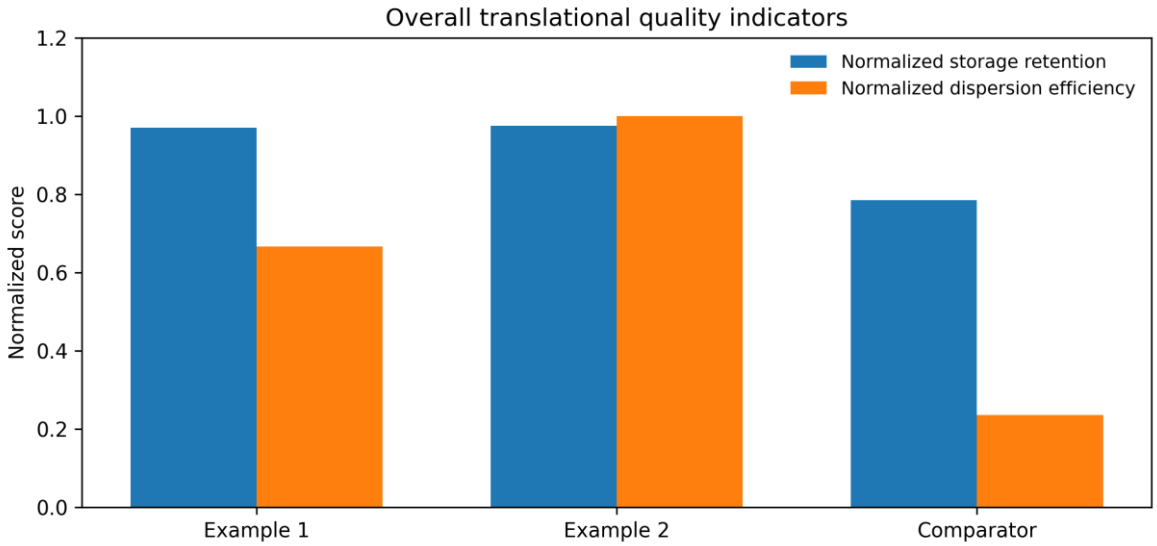

Figure 5. Overall translational quality indicators derived from the bench dataset.

3.2. Published clinical trial evidence matched to the current system

When we matched these bench findings to published human data, three evidence streams were most supportive. First, the lysine-calcium axis showed a direct human absorption signal. In 45 osteoporotic patients, short-term L-lysine supplementation (800 mg/day) significantly increased intestinal 47Ca absorption and improved renal calcium conservation, whereas comparator amino acids did not [2]. In a later clinical study of 24 osteopenic adults, calcium lysinate showed a reported relative oral bioavailability of 223.15% and a greater improvement in BMD T-score over 8 weeks than calcium carbonate or calcium citrate malate [3].

Second, the algae-derived calcium axis also showed clinically relevant signals. In 10 postmenopausal women, active absorbable algal calcium demonstrated significantly higher fractional calcium absorption than calcium carbonate (23.1 ± 6.4% vs 14.7 ± 6.4%, p = 0.006) when measured by a dual stable-isotope method [4]. In a double-blind crossover pilot trial of 12 fasting premenopausal women, Aquamin F, a marine algae-derived calcium product, produced greater urinary calcium clearance than placebo and more prolonged suppression of serum PTH than calcium carbonate after a meal challenge [5].

ISSN: 2710-0170

Third, the vitamin-guided utilization axis was supported, but with nuance. In older women, calcium plus vitamin D reduced PTH and bone-resorption markers over a short course of treatment [6]. In a dose-response trial of 76 healthy postmenopausal women, the highest vitamin D3 dose increased calcium absorption by an absolute 6.7%, confirming that vitamin status can modify calcium handling even when dietary calcium intake is not very low [7]. However, the cofactor story was not uniformly positive across all endpoints: in a 3-year randomized trial of 142 postmenopausal women with osteopenia, MK-7 markedly reduced undercarboxylated osteocalcin yet did not improve BMD or bone-turnover markers relative to placebo when both groups received calcium and vitamin D [8].

Table 2. Published human studies directly relevant to the current formulation logic

Study	Participants / design	Intervention	Key findings relevant to the current system
Civitelli et al., 1992	45 osteoporotic patients; comparative human metabolic study	L-lysine 800 mg/day vs comparator amino acids with 47Ca absorption assessment	L-lysine significantly increased intestinal calcium absorption and improved renal conservation of absorbed calcium [2].
Shankar et al., 2018	24 osteopenic adults; randomized open-label, 8 weeks	Calcium lysinate vs calcium carbonate vs calcium citrate malate	Relative oral bioavailability of calcium lysinate was reported as 223.15%; BMD T-score improvement was most pronounced in the calcium lysinate group [3].
Uenishi et al., 2010	10 postmenopausal women; stable-isotope comparison	Active absorbable algal calcium vs calcium carbonate	Fractional calcium absorption was 23.1 ± 6.4% with algal calcium vs 14.7 ± 6.4% with calcium carbonate ($p = 0.006$) [4].
Zenk et al., 2018	12 premenopausal women; double-blind crossover pilot	Aquamin F vs calcium carbonate vs placebo	Aquamin F produced greater urinary calcium clearance and more prolonged postprandial PTH suppression than placebo; calcium carbonate showed only an intermediate response [5].
Prestwood et al., 1996	12 older community-living women; clinical trial	Calcium 1200 mg/day plus vitamin D 800 IU/day	PTH and multiple bone-resorption markers decreased during treatment, while bone-formation markers remained unchanged [6].
Aloia et al., 2014	76 healthy postmenopausal women; randomized double-blind dose-response trial	Placebo vs vitamin D3 800, 2000, or 4000 IU/day for 8 weeks	A significant linear dose-response was observed; the highest vitamin D3 dose increased calcium absorption by an absolute 6.7% [7].

ISSN: 2710-0170

Study	Participants / design	Intervention	Key findings relevant to the current system
Rønn et al., 2021	142 postmenopausal women with osteopenia; 3-year randomized placebo-controlled trial	MK-7 375 μg/day vs placebo, both with calcium 800 mg/day and vitamin D3 38 μg/day	Undercarboxylated osteocalcin fell markedly in the MK-7 arm, but BMD and bone-turnover markers did not differ between groups [8].
Teucher et al., 2006	15 adults; randomized crossover trial	Calcium lactate drink with or without casein phosphopeptide-enriched preparations	Total absorbed calcium rose because more calcium was ingested, but fractional absorption was not meaningfully improved; investigators judged the difference biologically unimportant [9].
Umarji et al., 2021	Premenopausal Indian women; 6-month randomized controlled trial	Fortified supplement providing calcium, vitamin D, and vitamin K vs control	CTX fell by about 30%, PINP by about 20%, and the carboxylated/undercarboxylated osteocalcin ratio rose by about 60%, with good tolerability [10].

Not every cofactor candidate produced a favorable absorption signal. In a randomized crossover study in 15 adults, casein phosphopeptide-containing calcium drinks increased the total amount of absorbed calcium largely because they provided additional calcium, but fractional absorption was not meaningfully improved and the investigators concluded that the differences were unlikely to be biologically significant [9]. This negative finding is important for the present formulation because it indicates that inclusion chemistry alone is not sufficient; the broader microsphere and cofactor architecture likely matters more than any single excipient claim in isolation.

A broader nutritional trial also supports the relevance of combined calcium, vitamin D, and vitamin K exposure to bone turnover. In a 6-month randomized controlled trial in premenopausal Indian women, a fortified nutritional supplement providing calcium, vitamin D, and vitamin K was associated with approximately 30% lower CTX, approximately 20% lower PINP, and an approximately 60% increase in the ratio of carboxylated to undercarboxylated osteocalcin, with good tolerability [10]. Taken together, these data suggest that human biology does support a coordinated calcium-plus-cofactor strategy, provided that the formulation achieves efficient delivery.

Table 3. Module-level interpretation of the matched human evidence

Formulation module	Human evidence direction	Interpretation for the present system
L-lysine-assisted absorption module	Direct supportive human evidence	Human studies support lysine as a plausible enhancer of intestinal calcium handling and renal calcium conservation [2,3].
Algae-derived calcium-source module	Supportive human evidence	Stable-isotope and crossover-marker studies favor algae-derived calcium over conventional calcium carbonate on fractional absorption or short-term calcium-metabolism markers [4,5].

ISSN: 2710-0170

Formulation module	Human evidence direction	Interpretation for the present system
Vitamin D2 / K2-directed utilization module	Partly supportive, endpoint-specific evidence	Calcium plus vitamin D lowers PTH and bone resorption; MK-7 improves osteocalcin carboxylation but may not shift BMD or turnover markers over the same interval [6-8].
CPP-containing inclusion module	Mixed to negative human evidence	Human crossover data do not support a material increase in fractional calcium absorption from CPP alone [9].
GABA-containing inclusion architecture	Direct human calcium-absorption evidence still limited	The translational role of GABA is currently better understood as part of the overall inclusion/tolerability design than as an independently verified calcium-absorption driver.

4. Discussion

We did not rely on elemental calcium content alone. Instead, we examined whether our formulation architecture is directionally consistent with what human trials have already established about calcium absorption and bone metabolism. On that standard, the evidence is supportive.

The lysine signal is especially important. Human data show that lysine can enhance intestinal calcium absorption and improve renal conservation of absorbed calcium [2]. That observation is directly aligned with the absorption-promoting intention of our formulation. The second supportive pillar is the algae-derived calcium literature, where both stable-isotope and crossover-marker studies favored algae-derived calcium over conventional calcium carbonate on fractional absorption or short-term calcium-metabolism markers [4,5]. The third pillar is the cofactor module: calcium plus vitamin D consistently modifies PTH and bone-turnover behavior [6,7], while vitamin K2 appears to improve osteocalcin carboxylation even when harder skeletal outcomes do not move in parallel over the same time frame [8].

At the same time, our evidence matching also highlights where restraint is necessary. We did not identify a completed human trial in which oral GABA was isolated as the primary determinant of enhanced calcium absorption. For that reason, the GABA component in the current system is best interpreted as part of the designed inclusion and tolerability architecture rather than as an independently proven calcium-absorption intervention. Likewise, casein phosphopeptide evidence remains mixed, and the negative crossover study argues against overstating that module on its own [9].

In our view, these strengths and limitations converge on one practical conclusion: the exact multi-component preparation should now be tested directly in a randomized human study. The most appropriate biological endpoints would be fractional calcium absorption, serum calcium excursion, PTH suppression, P1NP, CTX or NTX, and tolerability. Such a trial would determine whether the formulation-level advantages we observed at bench level can translate into clinically relevant gains in calcium handling and skeletal metabolism.

5. Conclusion

In this study, we showed that the NVTIA GABA-lysine calcium preparation combines strong formulation-performance characteristics with a human evidence profile that is directionally

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consistent with improved calcium handling. The most convincing published support comes from L-lysine-assisted calcium absorption, calcium lysinate bioavailability, algae-derived calcium delivery, and calcium/vitamin-guided modulation of PTH and bone turnover. The clinical literature is more cautious for isolated casein phosphopeptide effects and remains incomplete for oral GABA as a stand-alone calcium-absorption driver. Overall, the current evidence supports formal randomized evaluation of the full preparation as a differentiated calcium-absorption and bone-metabolism system.

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