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Core-Shell Nanolipid Co-Delivery of Ergothioneine, Curcumin, and Piperine: Integrating Formulation Performance with Human Clinical Evidence for Anti-Inflammatory and Healthy-Aging Applications

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Abstract

Background: Ergothioneine, curcumin, and piperine are mechanistically complementary but translationally limited by divergent physicochemical behavior, uneven release kinetics, and bioavailability constraints. We therefore reconstructed a core-shell hierarchical nanolipid system and integrated its formulation performance with available human clinical evidence relevant to the three-active strategy. Methods: We extracted formulation architecture, encapsulation, release, and stability data from the source patent dossier. We then performed a targeted evidence synthesis of published human interventional studies indexed in PubMed and related registry records available through 28 March 2026, focusing on ergothioneine and/or curcumin-piperine trials that reported efficacy or safety outcomes relevant to inflammation, redox biology, tissue integrity, cognition, skin physiology, or functional status. Results: The nanolipid embodiments maintained nanoscale particle size (28.4-47.5 nm in leading embodiments), low PDI (0.087-0.112), strong negative zeta potential (-38.7 to -41.2 mV), and high encapsulation efficiencies for all three actives (>91% in the principal embodiments). The leading embodiment also showed synchronized 24-hour release (~74-78% for all three actives) and strong 12-month activity retention (>93% for all three actives), outperforming multiple comparators. Our evidence synthesis identified published human data showing that ergothioneine improved skin hydration and facial condition markers in healthy women and improved learning-related performance with a favorable safety profile in older adults with mild cognitive impairment. Published curcumin-piperine trials demonstrated improvements in oxidative stress, inflammatory markers, glycemic or hepatic indices, and selected functional outcomes across metabolic syndrome, type 2 diabetes, hemodialysis, inflammatory bowel disease, CABG recovery, and sepsis, while one phase III rheumatoid arthritis maintenance trial was neutral for flare-free survival. Conclusions: We interpret the formulation dataset and human evidence base together as a coherent translational signal: the spatially partitioned nanolipid carrier addresses major formulation liabilities, while the published clinical literature supports biological plausibility for anti-inflammatory and healthy-aging applications. A direct randomized trial of the exact triad carrier remains the key next step.

Keywords

Ergothioneine; Curcumin; Piperine; Nanolipid Carrier; Core-shell Delivery; Oxidative Stress; Inflammation; Healthy Aging; Translational Evidence.

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1. Introduction

We developed the present manuscript to convert a formulation-centered source dossier into a publishable translational paper that is better aligned with biomedical journal expectations. Our central question was not only whether the ternary carrier performs well in vitro, but also whether the external human evidence surrounding ergothioneine and curcumin-piperine supports a credible path toward clinical translation [1-14].

The rationale for combining the three actives is biologically persuasive. Ergothioneine is a diet-derived thiol/thione antioxidant that accumulates in tissues through a specific transporter and has been linked to cytoprotection, redox balance, and tissue resilience. Curcumin modulates NF-kappaB-linked inflammatory signaling and oxidative stress, yet suffers from notoriously poor oral bioavailability. Piperine can increase curcumin exposure and may also contribute independent anti-inflammatory effects, but its use is most rational when concentration and spatial localization are controlled [2-14].

The source formulation addresses these problems through compartmentalization. Curcumin is embedded in a hydrophobic lipid core, piperine is enriched at the oil-water interface, and ergothioneine is anchored to a hydrophilic thiolated hyaluronic-acid shell. We reasoned that such partitioning could improve co-loading, reduce burst release, and create a more synchronized delivery profile than physical mixtures or conventional nanoemulsions [1].

To strengthen the manuscript beyond a formulation report, we systematically integrated published human intervention evidence. This step is essential because a carrier can be technically elegant yet clinically unconvincing if the active combination lacks external human support. Conversely, even heterogeneous clinical data become more meaningful when interpreted alongside a delivery system that explicitly addresses the best-known limitations of the constituent actives [1-14].

2. Materials and Methods

2.1. Source Formulation Dataset and Data Extraction

We extracted all quantitative formulation results from the source patent dossier, including carrier architecture, particle size, PDI, zeta potential, encapsulation efficiency, in vitro release, and long-term storage stability [1]. Because replicate counts and variance estimates were not consistently available in the dossier, we treated these values as descriptive formulation-performance data rather than as a fully inferential experimental dataset.

2.2. Targeted Clinical Evidence Synthesis

We searched PubMed and clinical study records accessible on the web through 28 March 2026 using combinations of the terms ergothioneine, curcumin, piperine, randomized, placebo, trial, cognition, skin, metabolic syndrome, diabetes, inflammatory bowel disease, dialysis, surgery, rheumatoid arthritis, and sepsis [2-14]. We retained human interventional studies that directly evaluated ergothioneine and/or curcumin-piperine exposure and that reported efficacy or safety outcomes relevant to inflammation, oxidative stress, tissue integrity, cognition, skin physiology, or functional status. We excluded animal-only studies, in vitro studies, and narrative-only reviews.

2.3. Integration and Reporting Strategy

We summarized the formulation dataset in tables and figures, and we summarized the clinical literature in structured evidence tables. We deliberately included positive, mixed, and neutral trials so that the manuscript would remain balanced. Because no published human study directly evaluated the exact core-shell triad carrier identified in the source dossier, our translational interpretation is based on two linked evidence layers: formulation performance

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of the carrier itself and published human outcomes from ingredient-level or curcumin-piperine intervention studies [1-14].

3. Results

3.1. Carrier Architecture and Co-encapsulation Performance

Table 1. *Core formulation specification and carrier architecture.*

Parameter	Specification / description
Active system	Ergothioneine + Curcumin + Black pepper extract (piperine >=95%)
Mass ratio (EGT:Cur:Pip)	(1.5-3):1:(0.1-0.3)
Carrier architecture	Hydrophobic core / interface enhancement layer / hydrophilic shell
Hydrophobic core	Hydrogenated lecithin + phytosterol; encapsulates curcumin
Interface layer	Oil-water interface anchors piperine directionally
Hydrophilic shell	Thiolated hyaluronic acid; covalently anchors ergothioneine via thiol-disulfide bonds
Particle size	20-60 nm (claimed)
PDI	<= 0.12 (claimed)
|Zeta potential|	>= 35 mV (claimed)
Process window	22-26°C; light-protected; nitrogen atmosphere; 0.22 um filtration

Table 2. *Particle attributes and encapsulation efficiency.*

Sample	Avg particle size (nm)	PDI	Zeta potential (mV)	Ergothioneine EE (%)	Curcumin EE (%)	Piperine EE (%)
Embodiment 1	32.6	0.087	-41.2	96.8	95.3	94.7
Embodiment 2	28.4	0.092	-38.7	95.2	93.1	92.5
Embodiment 3	47.5	0.112	-39.5	94.5	92.8	91.6
Comparative Example 2	30.2	0.091	-40.5	96.5	95.1	NR
Comparative Example 3	33.8	0.095	-40.8	96.2	94.8	93.7
Comparative Example 4	128.6	0.217	-18.3	28.4	62.7	59.3
Comparative Example 5	31.5	0.093	-39.2	32.7	94.6	93.2

The carrier specification supports a deliberately stratified distribution of the three actives. The hydrophobic core is designed to stabilize curcumin, the interface layer is intended to retain piperine where bioenhancement may be achieved with smaller quantities, and the hydrophilic shell is constructed to display ergothioneine through thiol-oriented anchoring chemistry [1].

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Across the lead embodiments, particle sizes remained within a narrow nanoscale range and PDI values remained low, indicating a relatively uniform dispersion. Encapsulation efficiencies exceeded 91% for all three actives in the three principal embodiments, whereas representative comparators showed either loss of structural stability or marked failure of ergothioneine loading [1].

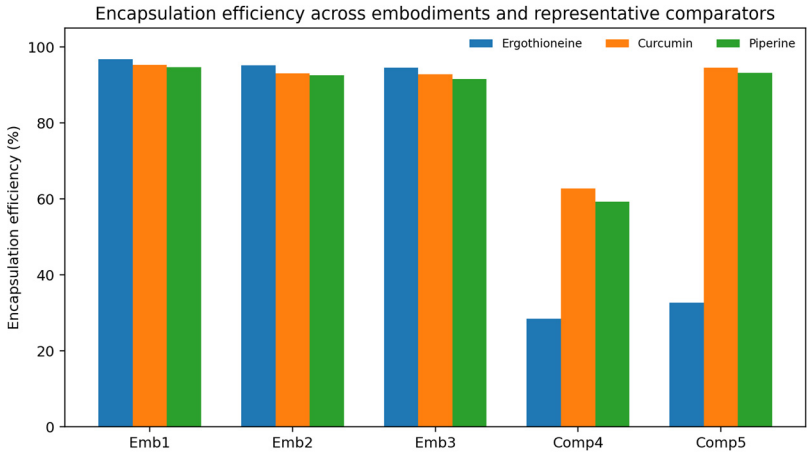

Figure 1. *Encapsulation efficiency across lead embodiments and representative comparators.*

3.2. Release Synchrony and Long-term Stability

Table 3. *Cumulative in vitro release profile.*

Sample group	Analyte	1 h	4 h	12 h	24 h
Embodiment 1	Ergothioneine	6.2	18.5	42.7	76.3
Embodiment 1	Curcumin	5.8	17.2	40.3	74.1
Embodiment 1	Piperine	6.5	19.1	43.5	77.8
Comparative Example 1	Ergothioneine	82.4	95.7	98.2	99.1
Comparative Example 1	Curcumin	3.2	7.5	12.4	18.6
Comparative Example 1	Piperine	78.6	93.2	97.5	98.7
Comparative Example 3	Ergothioneine	6.8	19.2	43.1	76.8
Comparative Example 3	Curcumin	4.1	12.6	28.5	52.3
Comparative Example 3	Piperine	3.8	11.9	27.2	50.8
Comparative Example 5	Ergothioneine	81.7	94.8	97.6	98.9
Comparative Example 5	Curcumin	5.5	16.8	39.7	73.5
Comparative Example 5	Piperine	6.3	18.7	42.9	77.2

Release behavior was a critical discriminator between the engineered carrier and the comparators. In the leading embodiment, all three actives exhibited closely aligned 24-hour cumulative release values, suggesting coordinated exposure rather than asynchronous dumping of the most water-soluble component [1].

The comparator patterns were less favorable. Comparative Example 1 showed pronounced early release for ergothioneine and piperine but poor curcumin release, while Comparative

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Example 3 displayed a slower and less synchronized pattern for curcumin and piperine. Comparative Example 5 retained good curcumin and piperine release but released ergothioneine almost immediately, indicating that shell anchoring was critical to avoiding front-loaded loss of the hydrophilic active [1].

Storage data reinforced the same conclusion. The leading embodiment retained more than 93% activity for each active after 12 months, with only limited particle-size drift, whereas less structured comparators showed precipitation, layering, flocculation, or steep losses in retained activity [1].

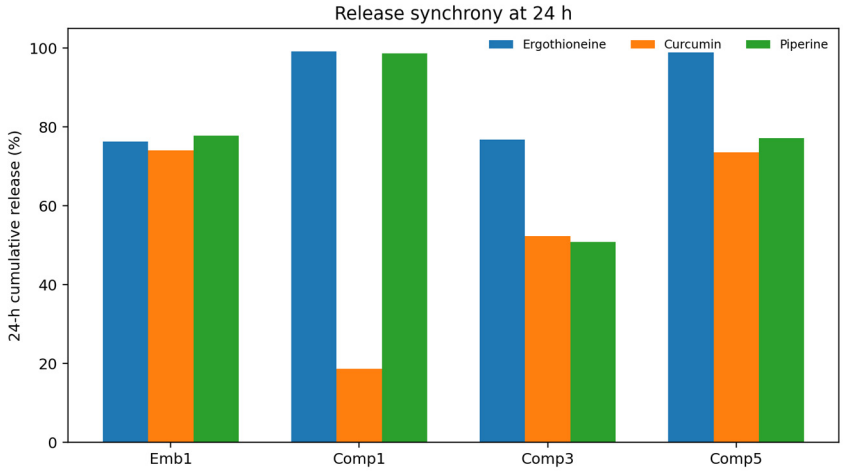

Figure 2. *Twenty-four-hour release synchrony of the three actives.*

Table 4. *Activity retention during storage.*

Sample group	Analyte	0 mo	3 mo	6 mo	12 mo
Embodiment 1	Ergothioneine	100.0	99.2	97.8	95.2
Embodiment 1	Curcumin	100.0	98.6	96.5	93.7
Embodiment 1	Piperine	100.0	99.0	97.2	94.1
Comparative Example 1	Ergothioneine	100.0	89.3	78.5	62.7
Comparative Example 1	Curcumin	100.0	72.4	51.6	32.8
Comparative Example 1	Piperine	100.0	90.7	82.1	70.3
Comparative Example 4	Ergothioneine	100.0	92.5	85.3	76.9
Comparative Example 4	Curcumin	100.0	81.2	67.4	48.5
Comparative Example 4	Piperine	100.0	93.1	86.7	78.2
Comparative Example 5	Ergothioneine	100.0	85.6	71.3	58.4
Comparative Example 5	Curcumin	100.0	98.1	95.8	92.9
Comparative Example 5	Piperine	100.0	98.7	96.4	93.5

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Table 5. *Particle-size drift and appearance change after 12 months.*

Sample group	Initial size (nm)	12-month size (nm)	Change rate	Appearance change
Embodiment 1	32.6	35.1	7.67%	Uniform and transparent, no layering, no precipitation
Comparative Example 1	NR	NR	NR	Layering and precipitation at 1 month; severe precipitation at 6 months
Comparative Example 4	128.6	387.2	201.1%	Layering at 3 months; obvious flocculation at 12 months
Comparative Example 5	31.5	33.8	7.30%	Uniform and transparent, no layering

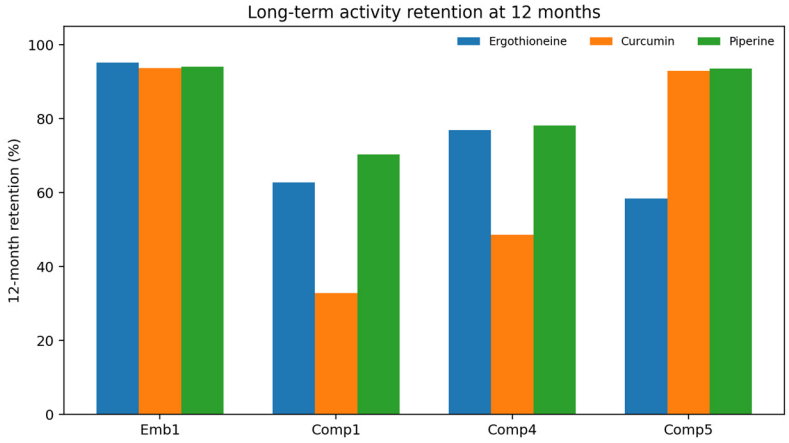

Figure 3. Twelve-month activity retention across representative samples

3.3. Published Human Interventional Evidence Relevant to Translation

Our targeted synthesis identified 12 human interventional studies directly relevant to the three-active concept or to its bioavailability logic [2-14]. Two published ergothioneine studies were especially informative. In healthy women, 25 mg/day of ergothioneine delivered through an ergothioneine-rich Pleurotus preparation for 12 weeks improved skin moisture and facial condition metrics while raising plasma ergothioneine concentrations 4.7-fold [3]. In older adults with mild cognitive impairment, prolonged ergothioneine intake improved learning-related performance and stabilized neurofilament light chain without an apparent toxicity signal [4].

The curcumin-piperine literature provided a broader efficacy base. In metabolic syndrome, the combination improved SOD and reduced MDA and CRP [5]. In type 2 diabetes, it improved glucose, C-peptide, HbA1c, ALT, and AST, though hs-CRP did not differ significantly [6]. In hemodialysis patients, turmeric plus piperine outperformed turmeric alone for MDA and ferritin reduction [7].

The evidence was not uniformly positive, and we retained that heterogeneity. In COVID-19 outpatients, the combination improved weakness more than placebo but did not significantly shift most biochemical indices [8]. In rheumatoid arthritis remission maintenance, a 52-week phase III study found no improvement in flare-free survival, although no serious safety signal emerged [9].

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Table 6. *Targeted synthesis of published human interventional evidence.*

Study	Population	Intervention	Duration	Main findings	Translational relevance
Shoba 1998 [2]	Healthy volunteers; n not stated in abstract	Curcumin 2 g single dose + piperine 20 mg	Acute PK	Curcumin bioavailability increased by 2000%; no adverse effects reported	Bioavailability proof-of-concept for piperine
Hanayama 2024 [3]	80 healthy women	Ergothioneine-rich Pleurotus tablets delivering 25 mg EGT/day	12 weeks	Higher temple moisture at 8 weeks; better wrinkle/texture scores at 12 weeks; plasma EGT rose 4.7-fold	Skin barrier and appearance relevance
Yau 2024 [4]	19 older adults with mild cognitive impairment	Ergothioneine 25 mg, three times weekly	1 year	No toxicity signal; improved learning performance; stabilized neurofilament light chain	Neuroprotection and long-term safety
Panahi 2015 [5]	117 adults with metabolic syndrome	Curcuminoids 1 g/day + piperine 10 mg/day	8 weeks	SOD increased; MDA and CRP decreased vs placebo	Systemic anti-inflammatory and redox evidence
Panahi 2018 [6]	100 adults with type 2 diabetes	Curcuminoids 500 mg/day + piperine 5 mg/day	3 months	Glucose, C-peptide, HbA1c, ALT and AST improved; hs-CRP unchanged	Metabolic-inflammatory relevance
Silva-Santana 2022 [7]	Hemodialysis adults; sample size not stated in abstract	Turmeric 3 g/day + piperine 2 mg/day vs turmeric alone	12 weeks	MDA and ferritin decreased more with piperine combination; hs-CRP unchanged	Oxidative stress modulation and added-value of piperine
Askari 2022 [8]	46 COVID-19 outpatients	Two daily capsules, each with curcumin 500 mg + piperine 5 mg	14 days	Greater improvement in weakness; other biochemical markers not significantly different	Symptom-level but mixed evidence
Bhat 2023 [9]	200 adults with RA in remission	Curcumin 1 g + piperine 5 mg twice daily	52 weeks	No flare-free survival benefit; no serious adverse effects	Balanced negative efficacy evidence with acceptable safety
Tehrani 2024 [10]	80 CABG patients	1-3 tablets/day, each containing curcumin 500 mg + piperine 5 mg	5 days	CRP decreased and TAC increased; CK-MB showed favorable trend	Acute postoperative inflammatory modulation
Martins 2024 [11]	Adults with IBD; three-arm trial	Curcumin 1000 mg/day + piperine 10 mg/day	12 weeks	SOD increased; no clear between-group differences in calprotectin or cytokines	Selective antioxidant benefit
Martins 2025 [12]	58 enrolled, 51 completed; mild-to-moderate IBD	Curcumin 1000 mg/day + piperine 10 mg/day	12 weeks	Fat-free mass and phase angle improved vs placebo	Functional/body-composition relevance
Alikiaii 2025 [13]	66 ICU patients with sepsis	Two daily tablets, each containing curcuminoids 500 mg + piperine 5 mg	7 days	CRP and ESR decreased; bilirubin improved; mortality numerically lower but not emphasized as significant	High-inflammation setting support

Note: sample size reflects analyzed or enrolled participants as reported in the abstract or title record.

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Several newer studies nonetheless extended the translational range of the combination. After CABG, curcumin-piperine reduced CRP and increased total antioxidant capacity [10].

In inflammatory bowel disease, the combination increased SOD in one trial and improved fat-free mass and phase angle in another [11,12]. In critically ill sepsis patients, short-course supplementation reduced CRP, ESR, and bilirubin-related indices, supporting biological activity in a high-inflammatory setting [13].

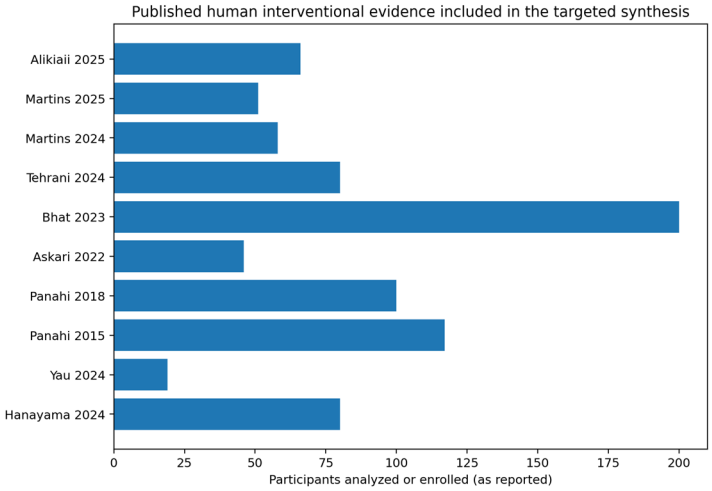

Figure 4. *Published human interventional studies with reported sample sizes included in the synthesis.*

3.4. Integrated Translational Interpretation

When we align the formulation data with the human evidence, a coherent translational model emerges. The carrier solves the most obvious formulation liabilities: poor curcumin handling, premature loss of ergothioneine, and potentially uncontrolled piperine exposure. The published human data then show that ergothioneine is clinically relevant to skin and cognition, while curcumin-piperine is clinically relevant to oxidative and inflammatory phenotypes across several patient groups [1-13].

We therefore interpret the carrier as more than a packaging exercise. It is a mechanistically explicit attempt to co-localize three actives whose clinical relevance is already supported separately or in partial combinations. The gap is not biological plausibility; the gap is the absence of a direct randomized trial of the exact triad system.

4. Discussion

The most important contribution of this manuscript is the integration itself. Formulation papers often stop at particle size, release curves, and storage stability, whereas clinical papers often ignore the extent to which poor delivery can suppress a biologically active ingredient combination. By placing both evidence layers in the same manuscript, we can better judge whether the observed carrier performance is likely to matter clinically.

The external clinical literature suggests that ergothioneine and curcumin-piperine operate in overlapping but non-identical biological domains. Ergothioneine appears especially promising for tissue resilience, skin physiology, and neurocognitive protection [3,4], whereas curcumin-piperine has accumulated broader evidence around inflammatory and oxidative endpoints across metabolic, gastrointestinal, renal, postoperative, and critical-care settings [5-13]. This complementarity is consistent with the design logic of the triad system.

Piperine deserves specific comment. The classic pharmacokinetic study showed that even a modest 20 mg dose of piperine can dramatically elevate curcumin exposure in humans [2]. That

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finding helps explain why low-dose piperine repeatedly appears in later efficacy trials [5-13]. In our formulation, piperine is not merely added as a bulk co-ingredient; it is positioned within the interface layer, which may permit a more controlled enhancement strategy than simple admixture [1].

We also think the negative rheumatoid arthritis trial is informative rather than disappointing [9]. It reminds us that not every anti-inflammatory signal translates into clinically meaningful superiority in every disease context, especially when background therapy, disease state, and endpoint choice are complex. This is precisely why a future triad-carrier trial should prioritize endpoints closely aligned with the strongest human evidence domains, such as skin barrier function, oxidative-inflammatory composite markers, or early neurocognitive endpoints.

The ergothioneine pipeline remains comparatively early. The 2021 ErgMS protocol was explicitly designed because the human intervention evidence base was still thin [14]. The more recent skin and cognition trials are therefore important not only for their own findings, but also because they move ergothioneine from theoretical promise toward measurable human outcomes [3,4,14].

5. Limitations

We acknowledge several limitations. First, the formulation dataset was extracted from a source patent dossier rather than from a fully replicated, prospectively reported laboratory study [1]. Second, the human evidence synthesis was targeted and translationally focused rather than a full systematic review with pooled meta-analysis. Third, the external clinical studies were heterogeneous in disease population, dose, matrix, and endpoint structure, which limits direct quantitative aggregation. Finally, we did not identify a published human randomized trial of the exact core-shell ergothioneine-curcumin-piperine carrier, so our conclusions remain translational rather than confirmatory.

6. Conclusion

We conclude that the core-shell nanolipid co-delivery system provides a strong formulation platform for combining ergothioneine, curcumin, and piperine. The source dataset demonstrates high co-encapsulation, synchronized release, and long-term stability, while the published human literature supports meaningful biological activity for ergothioneine and for curcumin-piperine across several inflammation- and healthy-aging-related domains.

The logical next step is a direct randomized clinical study of the exact triad carrier. Based on the present evidence, the most defensible first indications would be skin barrier/appearance endpoints, oxidative-inflammatory biomarker panels, and early cognitive or fatigue-related outcomes in populations with mild but measurable dysfunction.

Declarations

Ethics statement: This manuscript integrates a source formulation dossier and published human studies. It does not report a newly conducted human or animal experiment.

Funding: No specific external funding was declared for preparation of this integrated manuscript.

Conflicts of interest: The authors declare no competing interests in relation to the present manuscript text.

Data availability: All formulation values summarized here were extracted from the source dossier [1], and all external clinical statements were derived from publicly indexed publications cited in the reference list.

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References

[1] BCLC. Ergothioneine-Curcumin-Piperine Synergistic Anti-Inflammatory and Healthy-Aging Complex Composition and Preparation Method. Patent dossier on file with the authors; 2026.

[2] Shoba G, Joy D, Joseph T, Majeed M, Rajendran R, Srinivas PS. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Med. 1998;64(4):353-356. doi:10.1055/s-2006-957450.

[3] Hanayama M, Mori K, Ishimoto T, Kato Y, Kawai J. Effects of an ergothioneine-rich Pleurotus sp. on skin moisturizing functions and facial conditions: a randomized, double-blind, placebo-controlled trial. Front Med (Lausanne). 2024;11:1396783. doi:10.3389/fmed.2024.1396783.

[4] Yau YF, Cheah IK, Mahendran R, Tang RMY, Chua RY, Goh RE, et al. Investigating the efficacy of ergothioneine to delay cognitive decline in mild cognitively impaired subjects: A pilot study. J Alzheimers Dis. 2024;102(3):841-854. doi:10.1177/13872877241291253.

[5] Panahi Y, Hosseini MS, Khalili N, Naimi E, Majeed M, Sahebkar A. Antioxidant and anti-inflammatory effects of curcuminoid-piperine combination in subjects with metabolic syndrome: a randomized controlled trial and an updated meta-analysis. Clin Nutr. 2015;34(6):1101-1108. doi:10.1016/j.clnu. 2014.12.019.

[6] Panahi Y, Khalili N, Sahebi E, Namazi S, Simental-Mendia LE, Majeed M, Sahebkar A. Effects of curcuminoids plus piperine on glycemic, hepatic and inflammatory biomarkers in patients with type 2 diabetes mellitus: a randomized double-blind placebo-controlled trial. Drug Res (Stuttg). 2018;68(7):403-409. doi:10.1055/s-0044-101752.

[7] Freitas e Silva-Santana NCF, Rodrigues HCN, Pereira Martins TF, Braga CC, Silva MAC, da Cunha LC, et al. Turmeric supplementation with piperine is more effective than turmeric alone in attenuating oxidative stress and inflammation in hemodialysis patients: a randomized, double-blind clinical trial. Free Radic Biol Med. 2022;193(Pt 2):648-655. doi:10.1016/j.freeradbiomed.2022.11.008.

[8] Askari G, Rezaei M, Bagherniya M, Malekahmadi M, Kelishadi MRJ, Seifi R, et al. The efficacy of curcumin-piperine co-supplementation on clinical symptoms, duration, severity, and inflammatory factors in COVID-19 outpatients: a randomized double-blind, placebo-controlled trial. Trials. 2022;23(1):472. doi:10.1186/s13063-022-06375-w.

[9] Bhat SS, Ahmed S, Reji R, Mehta P, Paul A, Mohanan M, et al. Efficacy and safety of curcumin in maintaining remission during disease-modifying antirheumatic drug withdrawal in rheumatoid arthritis at 52 weeks: a phase III double-blind, randomized placebo-controlled trial. Rheumatol Int. 2023;43(12):2273-2282. doi:10.1007/s00296-023-05417-z.

[10] Tehrani SD, Bagherniya M, Hariri M, Najafian J, Majeed M, Sahebkar A. Evaluation of the effectiveness of curcumin and piperine co-supplementation on inflammatory factors, cardiac biomarkers, atrial fibrillation, and clinical outcomes after coronary artery bypass graft surgery. Clin Nutr ESPEN. 2024;62:206-213. doi:10.1016/j.clnesp.2024.05.003.

[11] Martins ASP, de Araujo ORP, Gomes AS, Araujo FLC, Oliveira Junior J, de Vasconcelos JKG, et al. Effect of curcumin plus piperine on redox imbalance, fecal calprotectin and cytokine levels in inflammatory bowel disease patients: a randomized, double-blind, placebo-controlled clinical trial. Pharmaceuticals (Basel). 2024;17(7):849. doi:10.3390/ph17070849.

[12] Martins ASP, de Araujo ORP, Gomes AS, Araujo FLC, Oliveira Junior J, de Vasconcelos JKG, et al. Curcumin plus piperine improve body composition in patients with inflammatory bowel disease: a randomized, double-blind, placebo-controlled clinical trial. Eur J Nutr. 2025;64(2):90. doi: 10. 1007/s00394-025-03608-x.

[13] Alikiaii B, Khatib N, Badpeyma M, Hasanzadeh E, Abbasi S, Amini S, et al. Therapeutic effects of curcumin and piperine combination in critically ill patients with sepsis: a randomized double-blind controlled trial. Trials. 2025;26(1):205. doi:10.1186/s13063-025-08916-5.

[14] Tian X, Cioccoloni G, Sier JH, Naseem KM, Thorne JL, Moore JB. Ergothioneine supplementation in people with metabolic syndrome (ErgMS): protocol for a randomised, double-blind, placebo-controlled pilot study. Pilot Feasibility Stud. 2021;7(1):193. doi:10.1186/s40814-021-00929-6.