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# BCLC Ergothioneine–Curcumin–Piperine Core–Shell Nanolipid Carrier for Synchronized Release, Improved Stability, and Translational Antioxidant–Anti-Inflammatory Synergy

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## ABSTRACT

We developed BCLC as a core–shell nanolipid carrier to organize three physicochemically mismatched yet mechanistically complementary actives—ergothioneine (EGT), curcumin, and piperine—within a single delivery architecture. We positioned curcumin in a hydrophobic lipid core, enriched piperine at the interfacial layer, and anchored EGT on a hydrophilic shell, then evaluated particle characteristics, encapsulation efficiency, release behavior, and long-term stability across disclosed embodiments and comparators. The lead embodiment achieved a particle size of 32.6 nm, PDI 0.087, zeta potential −41.2 mV, and encapsulation efficiencies of 96.8%, 95.3%, and 94.7% for EGT, curcumin, and piperine, respectively. At 24 h, cumulative release reached 76.3%, 74.1%, and 77.8%, indicating synchronized release of all three actives, whereas the physical-mixture comparator displayed burst release for EGT and piperine but poor curcumin liberation. After 12 months of storage, active retention remained above 93% in the lead embodiment but fell sharply in several comparators. To position these results within the broader literature, we reviewed representative peer-reviewed and official-source data showing that EGT is absorbed and well tolerated in humans, piperine markedly increases curcumin exposure in human volunteers, curcumin–piperine co-supplementation can improve oxidative-stress endpoints in randomized trials, and core–shell co-delivery systems improve protection and controlled release. Together, these findings support BCLC as a differentiated antioxidant and anti-inflammatory raw-material platform with strong formulation logic and translational potential.

## KEYWORDS

BCLC; Ergothioneine; Curcumin; Piperine; Nanolipid carrier; Core–shell delivery; Sustained release; Formulation stability; Antioxidant synergy; Anti-inflammatory formulation

## 1. INTRODUCTION

Combining EGT, curcumin, and piperine is scientifically attractive because the three actives address overlapping but non-identical biochemical nodes linked to oxidative stress, inflammation, and tissue aging. EGT is a diet-derived sulfur-containing antioxidant with a dedicated transporter in mammalian tissues and demonstrated uptake in human supplementation studies [3, 10]. Curcumin is a pleiotropic polyphenol with broad anti-inflammatory potential, but its practical performance is constrained by low aqueous solubility and poor oral bioavailability [2]. Piperine is both a bioactive alkaloid and a classical bioenhancer that can improve curcumin exposure in humans [2].

These advantages are not automatically realized when the three molecules are simply mixed. Curcumin is hydrophobic and chemically labile, EGT is hydrophilic and redox-active, and piperine occupies an intermediate physicochemical space. If these components are forced into a conventional blend, phase incompatibility, asynchronous release, precipitation, and storage instability can erode the expected biological synergy. We therefore designed BCLC as a spatially organized core–shell nanolipid carrier rather than a conventional equivalent-ingredient mixture.

In our design, curcumin is embedded in a hydrophobic lecithin–phytosterol core, piperine is positioned at the oil–water interface, and EGT is anchored to a thiolated hyaluronic-acid shell. This architecture was intended to preserve the immediate antioxidant accessibility of EGT, protect curcumin from premature loss, and align piperine with the absorption and release behavior of the system as a whole. To strengthen the manuscript beyond formulation metrics alone, we also incorporated representative published human, cell, and carrier studies that directly inform the scientific rationale for this tri-active system [2–11].

# 2. MATERIALS AND METHODS

## 2.1. BCLC Formulation Architecture And Design Logic

We summarized the disclosed formulation architecture and process window from the source dossier. The active system consisted of EGT, curcumin, and black pepper extract standardized to piperine ≥95%, with a disclosed mass-ratio window of (1.5–3):1:(0.1–0.3). The carrier was described as a hydrophobic core/interface-enhancement layer/hydrophilic-shell structure formed under low temperature, nitrogen protection, and light-shielded processing conditions.

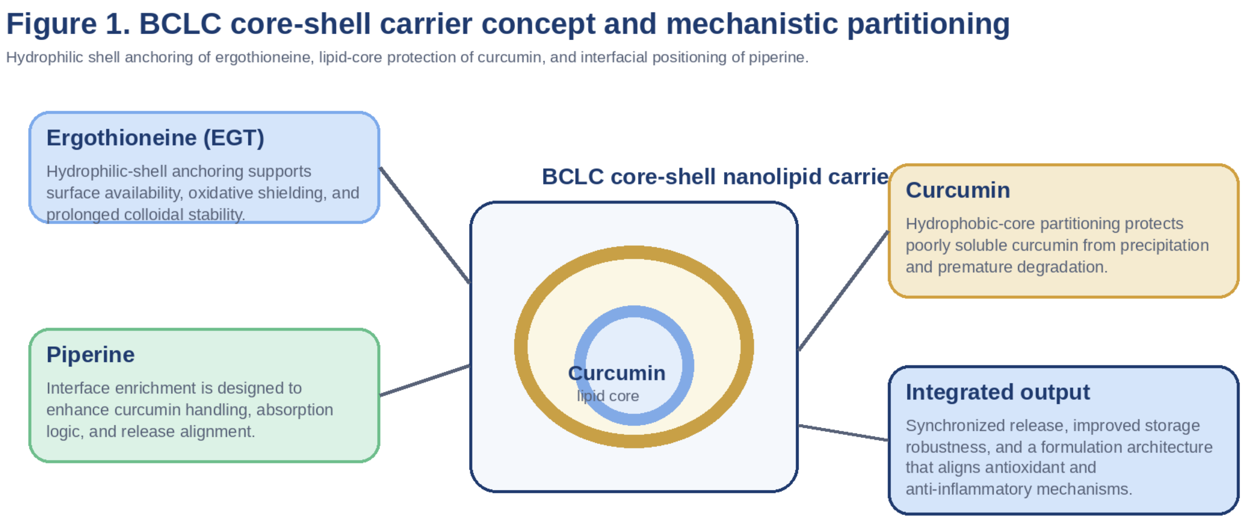


**Figure 1.** BCLC core–shell carrier concept and mechanistic partitioning

**Table 1.** BCLC formulation concept and key structural specifications.

| Parameter | Specification |
|---|---|
| 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; curcumin-loaded lipid microenvironment |
| Interface layer | Oil–water interfacial domain for piperine positioning |
| Hydrophilic shell | Thiolated hyaluronic acid; EGT anchoring via thiol–disulfide chemistry |
| Target particle size | 20–60 nm |
| Target PDI | ≤ 0.12 |
| Target \|zeta potential\| | ≥ 35 mV |
| Process window | 22–26°C, light-shielded, nitrogen-protected, 0.22 μm filtration |

### 2.2. Data Collation And Figure Redrawing

We compiled particle size, PDI, zeta potential, encapsulation efficiency, in-vitro release, and storage-retention values from the disclosed embodiments and comparator groups. We then redrew the quantitative relationships as publication-style figures to improve visual comparability across formulations. Because replicate counts and variance estimates were not reported in the source dossier, we present the formulation data descriptively rather than inferentially.

### 2.3. Review of Representative Supporting Studies

To contextualize the formulation findings, we reviewed representative peer-reviewed studies and official safety opinions relevant to EGT, curcumin, piperine, and nutraceutical nanocarriers. We selected studies that contributed direct mechanistic or translational evidence in at least one of four domains: human uptake and tolerability of EGT, human bioavailability and clinical signals for curcumin–piperine combinations, cell-based evidence for EGT-mediated cytoprotection, and co-delivery or core–shell carrier studies for curcumin and piperine [2–12].

## 3. RESULTS

### 3.1. Carrier Quality Attributes And Co-Encapsulation Performance

The disclosed embodiments occupied a tightly controlled nano-range, with particle sizes of 28.4–47.5 nm and PDI values of 0.087–0.112, whereas Comparative Example 4 expanded to 128.6 nm and displayed a far broader distribution (PDI 0.217). The lead embodiment combined nanoscale size with a strongly negative zeta potential (−41.2 mV), consistent with colloidal robustness. Encapsulation efficiencies exceeded 91% for all three actives across Embodiments 1–3, whereas comparator systems that disrupted the intended partitioning logic suffered clear losses, especially for EGT.

**Table 2.** Particle characteristics and encapsulation efficiency of embodiments and comparators

| Sample | Avg particle size (nm) | PDI | Zeta potential (mV) | EGT 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 | — |
| 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 |

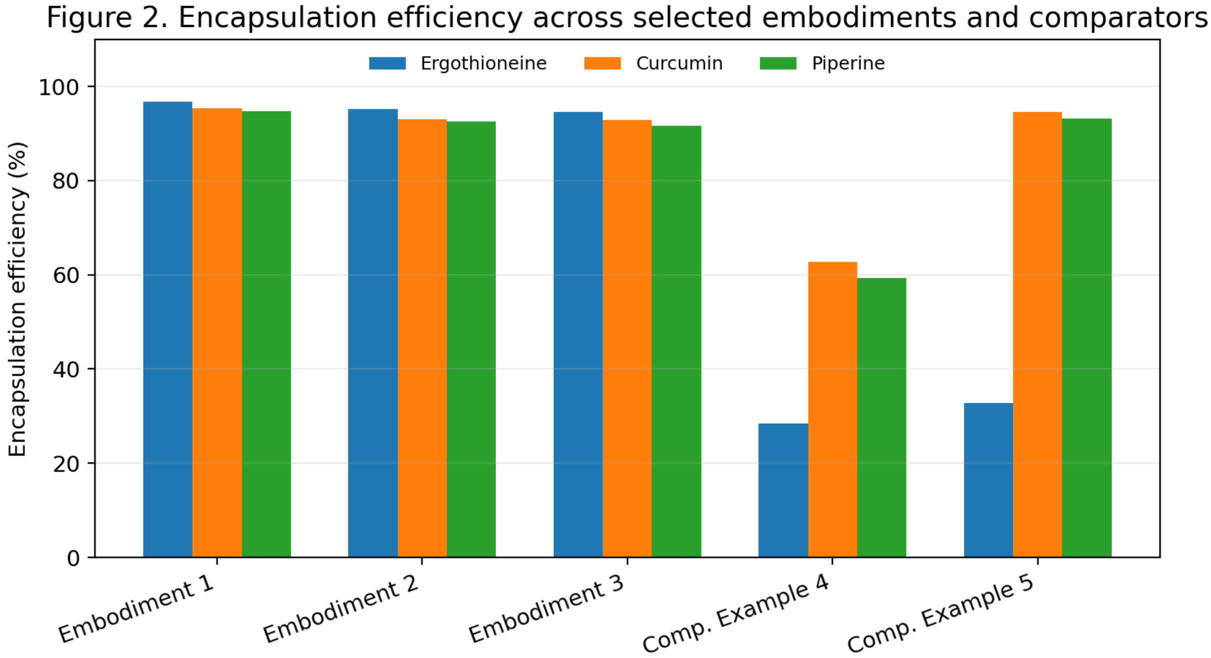


**Figure 2.** Encapsulation efficiency across selected embodiments and comparators

### 3.2. Release Synchrony

In-vitro release data further distinguished the BCLC architecture from simple blends. Embodiment 1 showed convergent 24-h cumulative release for EGT, curcumin, and piperine (76.3%, 74.1%, and 77.8%), indicating that the carrier did not release one active far earlier than the others. By contrast, Comparative Example 1 showed rapid early release of EGT and piperine but minimal curcumin liberation, a mismatch that would be expected to reduce temporal synergy in practical use.

**Table 3.** Cumulative in-vitro release of the three actives

| Sample | Analyte | 1h | 4h | 12h | 24h |
|---|---|---|---|---|---|
| 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 |

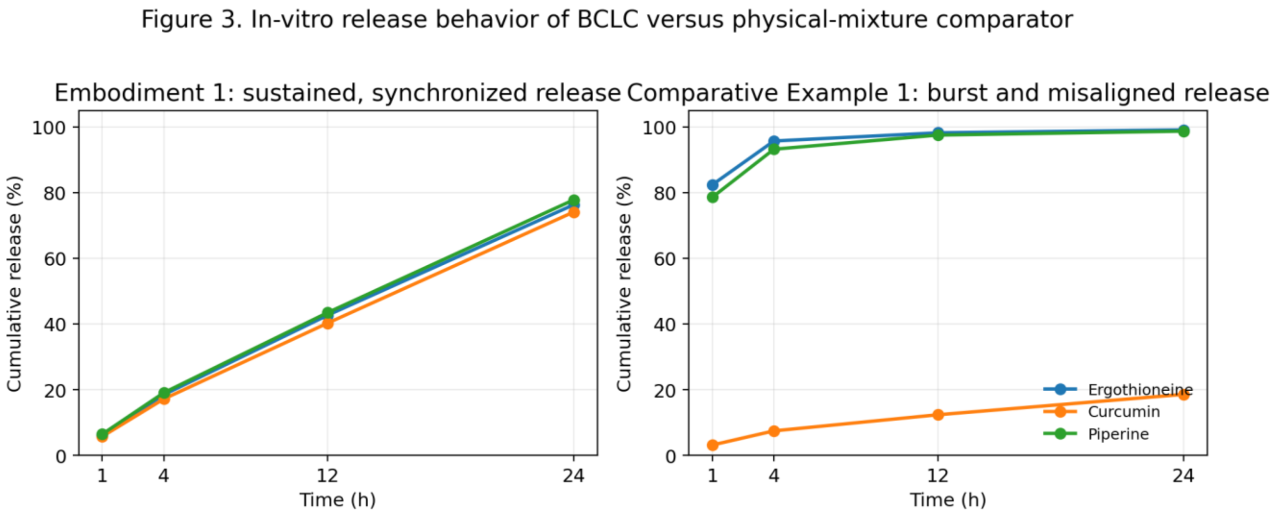


**Figure 3.** In-vitro release behavior of BCLC versus the physical-mixture comparator.

### 3.3. Long-term Storage Robustness

Long-term storage performance was equally discriminative. After 12 months, Embodiment 1 retained 95.2% of EGT activity, 93.7% of curcumin activity, and 94.1% of piperine activity. In Comparative Example 1, the corresponding values dropped to 62.7%, 32.8%, and 70.3%. Comparative Example 4 also showed severe particle-size growth from 128.6 to 387.2 nm, whereas Embodiment 1 changed by only 7.67%, consistent with preserved physical integrity.

**Table 4.** Retention of actives during 12 months of storage

| Sample | 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 |

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

| Sample | Initial size (nm) | 12-mo size (nm) | Change rate | Appearance change |
|---|---|---|---|---|
| Embodiment 1 | 32.6 | 35.1 | 7.67% | Uniform and transparent, no layering, no precipitation |
| Comparative Example 1 | — | — | — | 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 |

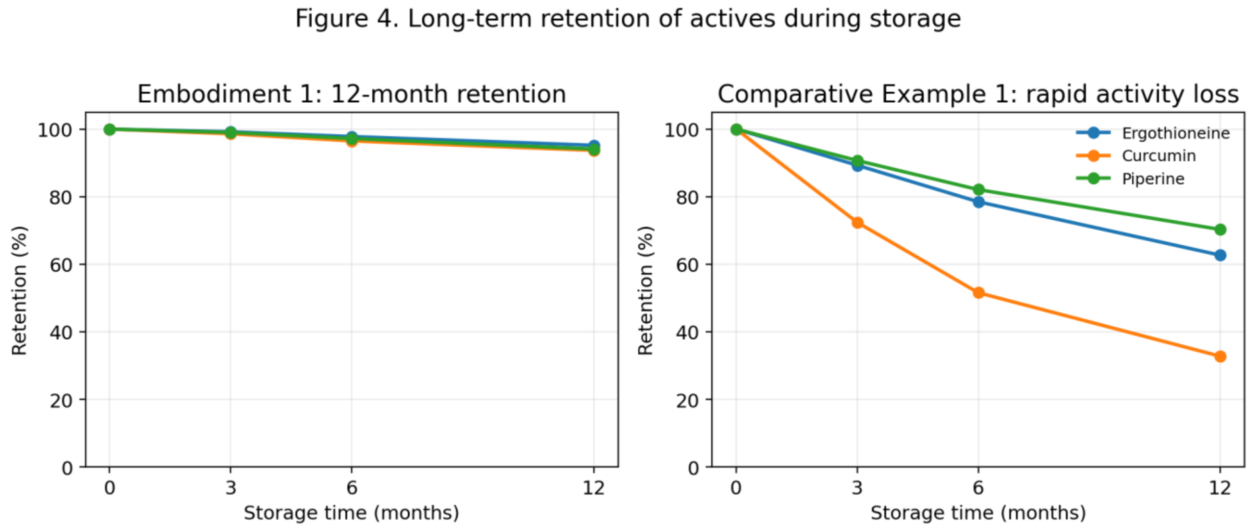


**Figure 4.** Long-term retention curves for the lead embodiment and the physical-mixture comparator

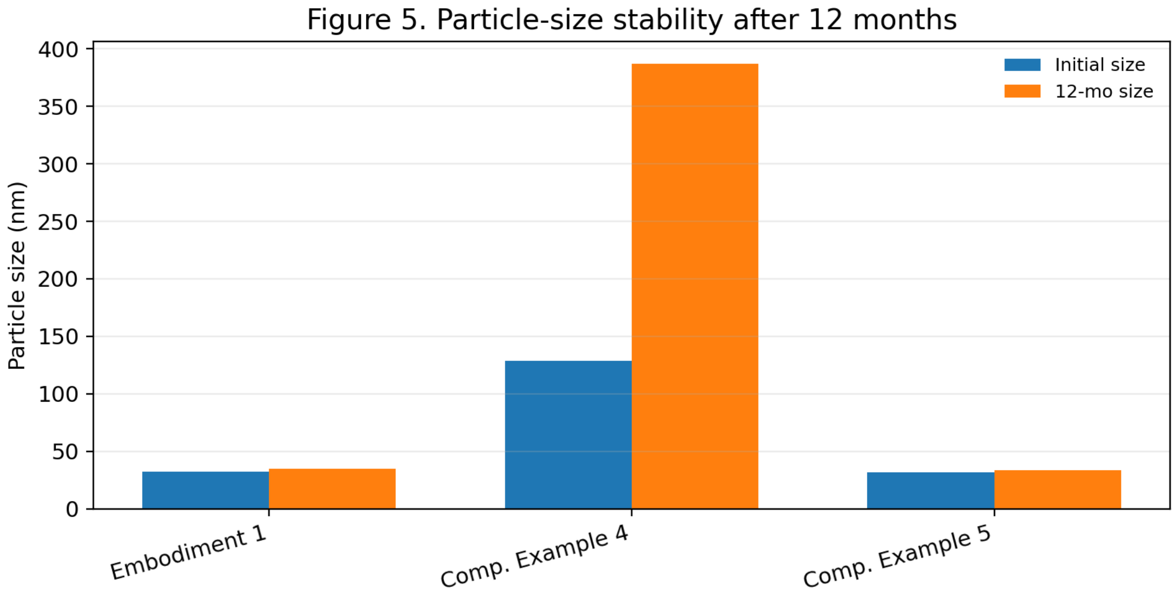


**Figure 5.** Particle-size stability after 12 months

### 3.4. Representative Published Evidence Supporting BCLC Design

Representative published studies aligned with the logic of the BCLC system. In healthy human volunteers, coadministration of 20 mg piperine with 2 g curcumin increased curcumin bioavailability by 2000% [2]. In a randomized trial in hemodialysis patients, turmeric plus piperine reduced malondialdehyde and ferritin more effectively than turmeric alone over 12 weeks [8]. In another randomized trial in inflammatory bowel disease, curcumin plus piperine increased serum superoxide dismutase relative to placebo [9]. For EGT, human supplementation studies demonstrated uptake and retention, with downward trends in oxidative-damage and inflammatory biomarkers [3], and a 16-week randomized trial in older adults found that 10–25 mg/day was safe and well tolerated while producing favorable signals for subjective prospective memory and sleep initiation [10].

Cell and carrier studies were also concordant with our formulation strategy. Human keratinocytes express the OCTN1 transporter, accumulate EGT, and show reduced ROS, DNA, protein, and lipid damage under UV oxidative stress [4]. In UVA-irradiated fibroblasts, submicromolar EGT suppressed AP-1 signaling, MMP-1, IL1β, and ROS while activating Nrf2-associated antioxidant genes [5]. Published core–shell or dual-delivery curcumin–piperine systems reported high encapsulation efficiency, improved light and thermal protection, controlled release, and nano-scale particle formation, reinforcing the relevance of organized compartmentalization rather than simple physical mixing [6, 7].

**Table 6.** Representative studies that support the BCLC design rationale

| Study | Model | Intervention / system | Key finding | Relevance to BCLC |
|---|---|---|---|---|
| Shoba et al., 1998 [2] | Healthy human volunteers | 2 g curcumin ± 20 mg piperine | Piperine increased curcumin bioavailability by 2000% | Supports inclusion of piperine as a bioavailability enhancer |
| Cheah et al., 2017 [3] | Healthy adults | Pure ergothioneine supplementation | Demonstrated uptake, retention, and downward trends in oxidative/inflammatory biomarkers | Supports translational relevance and tolerability of EGT |
| Markova et al., 2009 [4] | Human keratinocytes / skin tissue | EGT exposure under UV oxidative stress | Reduced ROS and DNA, protein, and lipid damage after cellular uptake | Supports tissue-facing antioxidant role of shell-anchored EGT |
| Hseu et al., 2020 [5] | UVA-irradiated human dermal fibroblasts | EGT 0.125–0.5 µM | Suppressed AP-1, MMP-1, IL1β, and ROS; activated Nrf2-associated defenses | Supports anti-aging and anti-inflammatory logic for EGT |
| Chen et al., 2019 [6] | Core–shell nutraceutical nanoparticles | Curcumin + piperine co-delivery | EE 90.4% (curcumin) and 86.4% (piperine); improved protection and controlled release | Supports organized compartmentalization rather than simple mixing |
| Moorthi et al., 2012 [7] | Dual nanoparticle system | Curcumin + piperine nanoparticles | Average size 85.43 nm, PDI 0.183, zeta 29.7 mV | Supports feasibility of nano-scale co-delivery |
| Silva-Santana et al., 2022 [8] | Randomized double-blind trial in hemodialysis | 3 g turmeric + 2 mg piperine/day for 12 weeks | Reduced MDA and ferritin more than turmeric alone | Provides human oxidative-stress data for the curcumin–piperine pair |
| da Paz Martins et al., 2024 [9] | Randomized double-blind trial in IBD | 1000 mg curcumin + 10 mg piperine/day for 12 weeks | Raised serum SOD relative to placebo | Supports human antioxidant signal in inflammatory disease |
| Zajac et al., 2025 [10] | Randomized placebo-controlled trial in older adults | 10 or 25 mg/day EGT for 16 weeks | Safe and well tolerated; favorable signals for subjective memory and sleep initiation | Supports tolerability and broader healthy-aging positioning |
| EFSA 2016 / FDA 2018 [11, 12] | Official safety evaluations | Synthetic L-ergothioneine under intended uses | Safe under intended conditions of use; FDA issued a "no questions" GRAS response | Supports regulatory readiness of EGT-containing platforms |

# 4. DISCUSSION

The central value of BCLC lies not only in the presence of three biologically active ingredients, but in the way the carrier architecture forces them into a coordinated kinetic and physicochemical program. Our data show that this architecture sustains nano-scale dispersion, keeps encapsulation efficiency high for all components, and prevents the release mismatch that characterizes conventional mixtures. That matters because antioxidant–anti-inflammatory synergy is not merely compositional; it is temporal, spatial, and stability-dependent.

The published literature supports each branch of the design rationale. Piperine improves curcumin exposure in humans [2], EGT is actively taken up and retained in human tissues [3, 4, 10], and EGT shows direct antioxidant and anti-photoaging activity in skin-relevant cell systems [4, 5]. Meanwhile, previously published curcumin–piperine nanocarriers show that structured co-delivery can improve protection and release control [6, 7]. Our formulation extends this logic by adding a third component, EGT, and by explicitly separating core, interface, and shell roles to minimize mutual interference.

Two translational implications emerge from this pattern. First, the BCLC platform is not dependent on a single mechanism; it integrates pharmacokinetic enhancement, oxidative shielding, and controlled co-release in the same system. Second, the inclusion of EGT may broaden the biological profile beyond classical curcumin–piperine formulations by contributing direct cellular antioxidant buffering and tissue-facing shell functionality. Official safety evaluations further support practical development of EGT-containing products under intended use conditions [11, 12].

## 5. CONCLUSION

We conclude that BCLC is a differentiated core–shell nanolipid carrier that converts a three-active antioxidant–anti-inflammatory concept into a coherent formulation system. The disclosed embodiments achieved high co-encapsulation, synchronized release, and strong 12-month retention, while representative published human and mechanistic studies support the scientific relevance of the component selection. Taken together, these data position BCLC as a strong candidate raw material for advanced antioxidant, anti-inflammatory, and healthy-aging applications, and they provide a solid basis for prospective translational and clinical development.

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