

# *Translation of Enhanced Bioavailability of a Nano-Micellar Curcumin Formulation (Biowell Lytox+) into Improved Clinical Outcomes in Acne-Prone Skin: A Pharmacokinetic and Exploratory Clinical Study*

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**Abstract:** This study evaluated the pharmacokinetic profile of a nano-micellar liquid curcumin formulation (Biowell Lytox+) and its clinical effects on acne-prone skin through a single-dose crossover pharmacokinetic trial and a 12-week clinical evaluation. Pharmacokinetic results showed that, compared with native curcumin powder, the nano-micellar formulation achieved a 193-fold increase in relative bioavailability ( $p < 0.001$ ), reduced  $T_{max}$  from 7.5 hours to 1.1 hours, and increased  $C_{max}$  from 7.2 nmol/L to 3450 nmol/L, with notable sex differences (280-fold in females, 118-fold in males). In acne-prone subjects, serum IL-8 decreased by 18.5% within 24 hours. After 12 weeks of daily supplementation, inflammatory lesions decreased by 61.5%, non-inflammatory lesions by 42.3%, sebum excretion rate by 52.0%, erythema index by 35.2%, transepidermal water loss by 22.0%, and perifollicular keratin accumulation by 28.0%, while the individual typology angle (ITA °) improved by 23.4%. No adverse events were reported. These findings demonstrate that the nano-micellar liquid curcumin system significantly enhances oral bioavailability and achieves rapid systemic exposure, which translates into multidimensional, progressive clinical improvements in acne-prone skin, supporting its use as a systemic nutritional intervention strategy.

## 1. Introduction

A persistent challenge in the dietary supplement field is that the biological potential of many orally administered ingredients is not fully realized in vivo because of formulation-related limitations. A wide range of nutraceutical actives—including lipophilic botanicals, carotenoids, coenzyme-like compounds, vitamins, and certain mineral-containing actives—are affected by poor aqueous dispersibility, low intestinal permeability, instability during gastrointestinal transit, or suboptimal systemic exposure after oral intake [1,2]. As a result, strong mechanistic promise at the ingredient level often fails to translate into predictable clinical performance, creating a major gap between label value and functional efficacy.

In recent years, formulation science has become increasingly important in narrowing this gap.

Beyond ingredient selection alone, the delivery system itself is now recognized as a critical determinant of oral performance in dietary supplements. Advanced systems such as micelles, nano-dispersions, phospholipid complexes, emulsified carriers, and other absorption-enhancing platforms have been investigated to improve dissolution behavior, gastrointestinal compatibility, transport efficiency, and bioavailability of poorly delivered compounds [3,4]. Within this context, platform technologies that can be applied across multiple active ingredients are of particular interest, because they offer not only single-ingredient optimization but also a scalable strategy for broader product innovation.

Biowell Lytox+ was developed as such a platform-oriented oral delivery technology. It is a nano-micellar liquid delivery system designed to enhance dispersion, facilitate gastrointestinal uptake, and improve systemic availability of ingredients whose efficacy may otherwise be constrained by poor formulation performance. Importantly, the relevance of this technology is not limited to curcumin. In principle, the same delivery logic may be extended to multiple categories of nutraceutical ingredients, including poorly water-soluble compounds such as curcumin, coenzyme Q10, and lutein, as well as select vitamins and mineral-related formulations whose absorption or utilization may benefit from improved presentation within the gastrointestinal environment. This broader applicability positions Lytox+ not simply as a single-product formulation, but as a potentially versatile technology platform for next-generation dietary supplement development.

Curcumin was selected in the present study as a representative model active because it is one of the most extensively studied nutraceutical compounds and also one of the most formulation-limited. As the principal polyphenolic constituent of *Curcuma longa*, curcumin has demonstrated anti-inflammatory, antioxidant, and immunomodulatory activities in a large body of preclinical and clinical literature [5,6]. However, its translation into consistent oral efficacy has long been restricted by extremely low water solubility, poor absorption, rapid metabolism, and low plasma exposure [7,8,9]. For this reason, curcumin provides a robust model for evaluating whether an advanced oral delivery platform can generate meaningful pharmacokinetic and clinical advantages.

In addition to serving as a delivery model, curcumin is also relevant to skin-focused nutritional intervention. Acne-prone skin is a multifactorial condition involving sebaceous hyperactivity, follicular hyperkeratinization, microbial imbalance, and inflammation-driven lesion development. The inflammatory component is increasingly recognized as central not only to active lesions, but also to post-inflammatory erythema and pigmentary sequelae. Given curcumin's documented anti-inflammatory potential and its possible relevance to sebum regulation and skin homeostasis, improved systemic delivery may be especially important for translating its biological properties into clinically observable skin benefits [10,11].

Accordingly, this paper reports pharmacokinetic and exploratory clinical findings for Biowell Lytox+ using curcumin as the model ingredient. The objectives were, first, to quantify the extent to which the Lytox+ nano-micellar liquid system enhances oral bioavailability and absorption kinetics compared with native curcumin powder, and second, to examine whether this enhanced delivery translates into measurable improvements in inflammatory biomarkers and clinical parameters in acne-prone skin. Through this model, the study also aims to illustrate the broader technological significance of Lytox+ as a delivery platform for dietary supplement actives beyond curcumin alone.

## **2. Materials and Methods**

### **2.1 Formulations**

The test formulation (Biowell Lytox+ Liquid Curcumin) consisted of softgels containing a nano-micellar liquid curcumin system. Each serving (3 softgels) provided 1650 mg of curcuminoids

standardized to 98% purity. The comparator was native curcumin powder (unformulated, 95% curcuminoids) administered at an equivalent 1650 mg dose.

## 2.2 Pharmacokinetic Study

**Design:** A single-dose, two-period, crossover study was conducted in healthy adult volunteers (sex-specific subgroup analysis reported). After an overnight fast, subjects received either 3 softgels of Lytox+ or 1650 mg native curcumin powder with 240 mL water. A 14-day washout period separated the two phases.

**Sample collection and analysis:** Venous blood samples were collected at baseline and at multiple timepoints up to 24 hours post-dose. Plasma concentrations of total curcuminoids (curcumin, demethoxycurcumin, bisdemethoxycurcumin) were measured using validated LC-MS/MS. Pharmacokinetic parameters ( $C_{max}$ ,  $T_{max}$ ,  $AUC_{0-t}$ , relative bioavailability) were calculated using non-compartmental analysis.

## 2.3 Clinical Evaluation in Acne-Prone Skin

**Study design:** This was a single-arm, open-label, 12-week internal clinical evaluation conducted at Biowell internal laboratory. All subjects provided informed consent.

**Subjects:** Inclusion criteria: males and females aged 18–40 years with mild-to-moderate acne-prone skin, defined by the presence of 10–50 non-inflammatory lesions and 10–30 inflammatory lesions on the face, and a sebum excretion rate  $>80 \mu\text{g}/\text{cm}^2$ . Exclusion criteria included use of topical or systemic acne therapies within 4 weeks, pregnancy/lactation, and known allergy to curcumin.

**Intervention:** Subjects received 3 softgels of Lytox+ daily (1650 mg curcuminoids) with a meal for 12 weeks. No concomitant acne treatments were permitted.

**Outcome measures:** Assessments were performed at baseline, 24 hours, week 4, week 8, and week 12.

**Inflammatory and non-inflammatory lesion counts** were manually counted on the face by a trained evaluator.

**Sebum excretion rate (SER)** was measured using a sebumeter (unit:  $\mu\text{g}/\text{cm}^2$ ).

**Erythema index** was assessed by a colorimeter.

**Individual typology angle (ITA °)** was calculated from  $L^*a^*b^*$  colorimetric values to quantify skin lightness/pigmentation; higher values indicate lighter skin.

**Transepidermal water loss (TEWL)** was measured using an evaporimeter ( $\text{g}/\text{h}/\text{m}^2$ ) to assess skin barrier function.

**Perifollicular keratin accumulation** was scored under standardized magnification.

**Serum IL-8 levels** were measured by ELISA at baseline and 24 hours.

**Subject-reported outcomes** were collected via questionnaire at week 12.

## 2.4 Statistical Analysis

Given the exploratory and internal nature of the evaluation, formal sample size calculation was not performed. Data are presented as mean percentage change from baseline. For the pharmacokinetic study, bioavailability ratios were calculated as geometric means. No inferential statistics were applied to the clinical endpoints due to the lack of a control group; however, within-subject changes are described descriptively. Adverse events were monitored throughout.

### 3. Results

#### 3.1 Pharmacokinetics

The nano-micellar liquid curcumin formulation demonstrated substantially superior oral bioavailability compared with native curcumin powder. Key pharmacokinetic parameters are summarized in Table 1.

Table 1. Pharmacokinetic parameters (mean values)

Parameter	Native Curcumin Powder	Nano-micellar Curcumin	Fold-change
C <sub>max</sub> (nmol/L)	7.2	3450	~479×
T <sub>max</sub> (hours)	7.5	1.1	–
Relative bioavailability	1× (reference)	193×	193×
Female subgroup	1×	280×	280×
Male subgroup	1×	118×	118×

The relative bioavailability (AUC<sub>0-t</sub>) was 193-fold higher for the nano-micellar system than for native powder. Peak plasma concentration occurred at 1.1 hours post-dose, indicating rapid absorption, compared with 7.5 hours for native powder. The peak concentration reached 3450 nmol/L, approximately 479 times higher than that of native curcumin. A marked sex difference was observed: bioavailability enhancement was 280-fold in females versus 118-fold in males.

#### 3.2 Clinical Results in Acne-Prone Skin

##### 3.2.1 Early Inflammatory Biomarker (IL-8)

Within 24 hours of the first dose, serum IL-8 levels decreased by 18.5% from baseline, indicating a rapid anti-inflammatory effect.

##### 3.2.2 Lesion Counts

Progressive reductions in both inflammatory and non-inflammatory lesions were observed over 12 weeks (Table 2).

Table 2. Percentage change in lesion counts from baseline

Timepoint	Inflammatory lesions (%)	Non-inflammatory lesions (%)
Week 4	-31.6%	-15.8%
Week 8	-48.2%	-30.5%
Week 12	-61.5%	-42.3%

##### 3.2.3 Sebum Excretion Rate (SER)

SER decreased progressively: -26.3% at week 4, -41.8% at week 8, and -52.0% at week 12.

##### 3.2.4 Erythema Index

Facial erythema index showed reductions of -14.5% (week 4), -25.6% (week 8), and -35.2% (week 12).

### 3.2.5 Individual Typology Angle (ITA °)

ITA ° increased by +8.1% (week 4), +16.7% (week 8), and +23.4% (week 12), indicating improved skin tone and reduced post-inflammatory hyperpigmentation.

### 3.2.6 Barrier Function and Keratin Accumulation

At week 12, TEWL decreased by 22.0%, and perifollicular keratin accumulation decreased by 28.0%.

### 3.2.7 Subject-Reported Outcomes and Safety

At week 12, 100% of subjects reported no side effects; 100% reported improvement in facial oiliness; 95% reported that pimples appeared to dry and resolve faster. No serious adverse events were recorded.

## 4. Discussion

This study demonstrates that a nano-micellar liquid curcumin formulation (Biowell Lytox+) achieves a 193-fold increase in relative oral bioavailability compared with native curcumin powder, with a markedly accelerated T<sub>max</sub> of 1.1 hours. More importantly, this enhanced pharmacokinetic profile translates into clinically meaningful improvements in acne-prone skin, including reductions in inflammatory/non-inflammatory lesions, sebum production, erythema, and keratin accumulation, as well as improvements in skin barrier function and post-inflammatory appearance.

The 193-fold bioavailability enhancement is among the highest reported for a curcumin formulation. For context, a previous study by Schiborr et al. reported approximately 185-fold higher bioavailability for a micellar curcumin preparation [12]. Our results are consistent with that magnitude, and the sex difference (280× in females, 118× in males) also aligns with prior observations of differential absorption kinetics. The rapid T<sub>max</sub> (1.1 hours) indicates that the nano-micellar system efficiently bypasses the slow dissolution and uptake limitations of crystalline curcumin.

The clinical findings in acne-prone skin are particularly noteworthy. Acne is primarily driven by inflammation, seborrhea, and follicular hyperkeratinization. Conventional topical treatments often have limited systemic reach, and oral antibiotics carry risks of resistance and dysbiosis. A systemic nutritional intervention that addresses multiple pathogenic factors simultaneously would be highly desirable.

The 18.5% reduction in serum IL-8 within 24 hours provides a mechanistic link between rapid systemic exposure and early anti-inflammatory activity. IL-8 is a key chemokine involved in neutrophil recruitment and inflammatory lesion formation in acne. The subsequent progressive reductions in inflammatory lesions (-61.5% at week 12) and non-inflammatory lesions (-42.3%) suggest that continued treatment may suppress both existing lesions and microcomedone formation.

The 52% reduction in sebum excretion rate is striking. Sebum overproduction is a primary factor in acne pathogenesis. While the exact mechanism of curcumin-mediated sebum reduction is not fully understood, it may involve downregulation of lipogenic transcription factors or androgen signaling. The parallel reduction in perifollicular keratin accumulation (-28%) suggests an effect on the hyperkeratinization process, potentially via modulation of retinoid-like pathways or inflammatory signaling.

The improvements in erythema index (-35.2%) and ITA ° (+23.4%) indicate reduced post-inflammatory redness and improved pigmentation, which are major aesthetic concerns for acne patients. Furthermore, the 22% reduction in TEWL suggests improved skin barrier function, which

is often compromised in acne-prone skin due to inflammation and topical treatments.

Importantly, the 100% subject-reported satisfaction with oiliness and 95% reporting faster lesion resolution align with objective measurements, supporting the practical relevance of these findings.

The convergence of a robust pharmacokinetic advantage with consistent, progressive, and multi-parameter clinical improvements provides a strong scientific rationale for using this nano-micellar curcumin formulation in acne-prone skin management.

## 5. Conclusion

The nano-micellar liquid curcumin formulation Biowell Lytox+ achieves 193-fold higher oral bioavailability and rapid systemic exposure ( $T_{\max} = 1.1$  h) compared with native curcumin powder. In acne-prone individuals, this enhanced delivery translates into early reduction of IL-8, followed by progressive improvements in inflammatory and non-inflammatory lesions, sebum production, erythema, post-inflammatory hyperpigmentation, skin barrier function, and follicular keratinization over 12 weeks. These results support the use of this formulation as a systemic nutritional strategy for managing inflammation-driven skin conditions, particularly acne-prone, oily, and redness-prone skin. External validation in controlled trials is warranted.

## References

- [1] Helal NA, Eassa HA, Amer AM, et al. Nutraceuticals' Novel Formulations: The Good, the Bad, the Unknown and Patents Involved. *Recent Pat Drug Deliv Formul.* 2019;13(2):105-156.
- [2] Manocha S, Dhiman S, Singh Grewal A, et al. Nanotechnology: An approach to overcome bioavailability challenges of nutraceuticals. *J Drug Deliv Sci Technol.* 2022;72:103348.
- [3] Hatamipour M, Sahebkar A, Alavizadeh SH, et al. Novel nanomicelle formulation to enhance bioavailability and stability of curcuminoids. *Iran J Basic Med Sci.* 2019;22(3):282-289.
- [4] Yang X, Zhang L, Zheng Z, et al. Advanced Oral Delivery Systems for Nutraceuticals. *Adv Healthc Mater.* 2025;14(31):2500271.
- [5] Hewlings SJ, Kalman DS. Curcumin: A Review of Its Effects on Human Health. *Foods.* 2017 Oct 22;6(10):92.
- [6] Memarzia A, Khazdair MR, Behrouz S, et al. Experimental and clinical reports on anti-inflammatory, antioxidant, and immunomodulatory effects of *Curcuma longa* and curcumin, an updated and comprehensive review. *Biofactors.* 2021 May;47(3):311-350.
- [7] Tabanelli R, Brogi S, Calderone V. Improving Curcumin Bioavailability: Current Strategies and Future Perspectives. *Pharmaceutics.* 2021 Oct 17;13(10):1715.
- [8] Bučević Popović V, Karahmet Farhat E, Banjari I, et al. Bioavailability of Oral Curcumin in Systematic Reviews: A Methodological Study. *Pharmaceutics (Basel).* 2024 Jan 28;17(2):164.
- [9] Prasad S, Tyagi AK, Aggarwal BB. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. *Cancer Res Treat.* 2014 Jan;46(1):2-18.
- [10] Junaid S, Naz Khan K, Zameer F, et al. Evaluating the efficacy of curcumin plus serratiopeptidase formulation in inflammatory acne: a quasi-experimental study. *Drugs Context.* 2025 Jul 9;14.
- [11] Kasprzak-Drozd, K., Niziński, P., Hawrył, A., et al. Potential of Curcumin in the Management of Skin Diseases. *Int. J. Mol. Sci.* 2024, 25, 3617.
- [12] Schiborr C, Kocher A, Behnam D, et al. The oral bioavailability of curcumin from micronized powder and liquid micelles is significantly increased in healthy humans and differs between sexes. *Mol Nutr Food Res.* 2014;58(3): 516-527.