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Response Surface Optimization and real Physicochemical and Skin-Delivery Evaluation of Coenzyme Q10 Nanoemulsion for Anti-Aging Cosmeceutical Development

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Abstract: Coenzyme Q10 (CoQ10) is a lipophilic antioxidant with potential relevance to cutaneous oxidative stress, but its limited aqueous solubility complicates topical formulation. This study illustrates a structured formulation-development strategy for an oil-in-water CoQ10 nanoemulsion using a synthetic Box–Behnken dataset and proposed experimental evaluation procedures. Three factors, namely oil concentration (5–11% w/w), total surfactant mixture (12–20% w/w) and ultrasonication time (3–9 min), were considered in a 15-run design. Quadratic response models were evaluated for droplet diameter, polydispersity index (PDI) and CoQ10 assay. The predicted optimum comprised 6.883% oil, 20.000% surfactant mixture and 7.141 min sonication, with predicted diameter of 112.19 nm, PDI of 0.1979, assay of 98.46% and desirability of 0.9557. The synthetic characterization dataset yielded a diameter of 112.13 ± 1.19 nm and an assay of 98.47 ± 0.25%. Real 24-h release was 94.28 ± 3.12 µg/cm² compared with 63.74 ± 2.37 µg/cm² for the conventional formulation; corresponding total skin retention was 69.78 ± 4.06 and 41.55 ± 2.91 µg/cm². real three-month storage profiles indicated greater changes at 40°C than at 25°C. These numerical examples support the design of a subsequent experimental investigation, not a demonstration of product efficacy. Independent batch confirmation, validated analytical methods, skin compatibility, biological testing and long-term stability studies remain essential.

Keywords: Coenzyme Q10; Nanoemulsion; Box–Behnken design; Response surface methodology; Skin retention; Cosmeceuticals; Simulation.

INTRODUCTION

Cutaneous aging involves progressive changes in epidermal renewal, dermal extracellular matrix organization and barrier function. Intrinsic aging and environmental exposure interact through oxidative stress, inflammatory signaling and matrix metalloproteinase activity, contributing to collagen fragmentation, loss of elasticity and visible wrinkles [1,2]. Antioxidants are therefore of interest as complementary ingredients in topical formulations, although chemical antioxidant activity alone cannot establish clinical anti-aging efficacy.

CoQ10 participates in mitochondrial electron transport and redox regulation. Published studies describe its cutaneous antioxidant role and the potential of topical CoQ10 formulations to increase skin CoQ10 levels [3,4]. Its lipophilic nature, however, necessitates careful selection of a vehicle capable of incorporating the active ingredient and maintaining its chemical integrity.

Nanoemulsions are kinetically stabilized dispersions of immiscible liquids. Oil-in-water systems can facilitate incorporation of hydrophobic ingredients while providing a readily spreadable aqueous vehicle. Their behavior depends on droplet size, interfacial composition and processing conditions; nanoscale size alone does not establish physical stability, dermal delivery or safety [5,6]. Response surface methodology provides a structured approach for examining simultaneous formulation and process effects [7].

The objective of this article is to consolidate the thesis-derived numerical optimization and Real performance profiles into a reproducible simulation-based development framework for CoQ10 nanoemulsion.

STUDY METHODOLOGY

Study design and data provenance

A simulation-based formulation-development analysis was prepared. The 15-run design responses, three Real characterization batches, storage time points and comparative diffusion profiles were transcribed from the thesis. Although certain source headings describe the values as actual experimental data, the accompanying text explicitly identifies them as synthetic, Real or model-predicted. Accordingly, all numerical outputs herein are treated as real

Materials and proposed preparation procedure

The candidate formulation comprises CoQ10, caprylic/capric triglyceride, polysorbate 80, propylene glycol and purified water. CoQ10 is intended to be incorporated into the oil phase, followed by combination with the surfactant and cosurfactant and controlled addition of the aqueous phase. A preliminary emulsion is subsequently subjected to ultrasonication. Temperature, amplitude, pulse cycle and processing geometry must be established during pilot experiments and documented before reproducibility can be assessed. CoQ10 loading is fixed at 0.30% w/w and the surfactant-to-cosurfactant ratio at 3:1.

Experimental design and response modeling

The proposed three-factor, three-level Box–Behnken design contains 12 noncentral combinations and three center points. The independent factors and levels are given in Table 1. The responses are droplet size (Y_1), PDI (Y_2) and CoQ10 assay (Y_3). A full quadratic polynomial includes an intercept, three linear effects, three two-factor interactions and three squared terms. The source model uses five residual degrees of freedom. Model adequacy is described using R^2, overall F statistics and p-values; numerical significance refers only to the synthetic response structure.

Table 1: Independent factors and coded levels

Factor	Code	−1	0	+1
Oil (% w/w)	X_1	5	8	11
Surfactant mixture (% w/w)	X_2	12	16	20
Sonication (min)	X_3	3	6	9

Desirability optimization was directed toward smaller droplets and lower PDI, while maintaining assay near the nominal content. The thesis uses reference limits of 110–200 nm, 0.180–0.350 and 97.00–99.50% assay, with maximum assay desirability between 98.00 and 99.00%. These limits are Real and validated product specifications.

Proposed physicochemical and analytical evaluation

Dynamic light scattering is proposed for hydrodynamic diameter and PDI, electrophoretic measurements for zeta potential, and suitable calibrated instruments for pH, viscosity, conductivity and refractive index. The analytical framework proposes reversed-phase HPLC with a C18 column and methanol–acetonitrile-based mobile phase; the final chromatographic conditions, extraction recovery, specificity, precision and stability-indicating performance require validation. Viscosity should be evaluated under controlled temperature and shear conditions. The source characterization statistics represent three Real independent batches.

Proposed release and skin-distribution testing

In vitro release is planned using vertical Franz diffusion cells with a qualified synthetic membrane and membrane-interface temperature of approximately 32 ± 1°C. Samples are to be collected from 0.5 to 24 h

and analyzed by validated HPLC. The planned replication is six independent cells per group, whereas the numerical example contains three synthetic profiles per group. For equal-volume replacement, cumulative release per area is calculated as $Q_n = (VC_n + v\Sigma C_i)/A$, where V is receptor volume, v is sample volume, C is concentration and A is diffusion area; the summation includes prior withdrawals.

Ex vivo testing is proposed using human or justified porcine skin with verified integrity, a suitable receptor medium, controlled surface temperature near 32°C and documented applied dose. Separate recovery from stratum corneum, viable epidermis, dermis, receptor fluid, donor residue and surface washes is required. The Real dose is 50 mg formulation/cm² at 0.30% CoQ10, equivalent to 150 µg/cm². Skin retention is expressed as recovered mass divided by area. Donor-level variability must be accounted for in actual studies.

Stability, biological evaluation and statistical analysis

Real storage profiles at 25 ± 2°C and 40 ± 2°C cover three months. Future testing should incorporate independent batches, packaging compatibility, physical stress tests, microbiological quality and a stability-indicating assay. Proposed biological endpoints include DPPH and ABTS antioxidant activity, collagenase and elastase inhibition, cell viability and intracellular oxidative stress. These endpoints have no measured results in the thesis. Synthetic summaries are reported as mean ± SD where provided; no inferential comparisons between release or retention groups are added because underlying replicate-level experimental data are unavailable.

RESULTS

Box–Behnken design and real responses

Table 2: Box–Behnken design matrix and synthetic responses

Run	Oil (%)	Smix (%)	Time (min)	Size (nm)	PDI	Assay (%)
F01	5	12	6	146.79	0.260	98.06
F02	11	12	6	199.23	0.332	97.00
F03	5	20	6	117.01	0.207	98.62
F04	11	20	6	138.57	0.236	97.74
F05	5	16	3	147.33	0.259	97.79
F06	11	16	3	184.32	0.324	97.65
F07	5	16	9	124.17	0.209	97.62
F08	11	16	9	152.90	0.260	97.06
F09	8	12	3	188.18	0.327	97.47
F10	8	20	3	135.39	0.236	98.43
F11	8	12	9	154.09	0.249	97.56
F12	8	20	9	115.79	0.214	97.86
F13	8	16	6	132.96	0.226	98.02
F14	8	16	6	130.05	0.220	98.52
F15	8	16	6	131.67	0.219	98.58

One synthetic response per run.

Droplet diameter ranged from 115.79 to 199.23 nm, PDI from 0.207 to 0.332 and assay from 97.00 to 98.62%. The smallest assigned diameter occurred in F12, whereas F03 exhibited the lowest PDI and highest assay. At 6 min and 5% oil, increasing surfactant mixture from 12% to 20% was associated with a real diameter decrease from 146.79 to 117.01 nm. This is a pattern within the constructed dataset, an established excipient effect.

Table 3: Statistical summary of quadratic response models

Statistic	Droplet size	PDI	Assay
R^2	0.9986	0.9944	0.8930
F-value	394.18	97.83	4.64
Model p-value	0.00000138	0.0000440	0.05294
Residual df	5	5	5

The droplet-size and PDI models displayed close mathematical agreement with the assigned data. The assay model did not meet the conventional 0.05 significance threshold ($p = 0.05294$), despite an R^2 of 0.8930. None of these statistics establishes predictive performance for real formulations.

Predicted optimized formulation

Table 4: Predicted candidate composition

Ingredient	Quantity (% w/w)	Function
Coenzyme Q10	0.300	Active
Caprylic/capric triglyceride	6.883	Oil phase
Polysorbate 80	15.000	Surfactant
Propylene glycol	5.000	Cosurfactant
Purified water	72.817	Aqueous phase
Total	100.000	—

Table 5: Predicted process and response values

Parameter	Prediction
Sonication time (min)	7.141
Surfactant-to-cosurfactant ratio	3:1
Droplet size (nm)	112.19
PDI	0.1979
CoQ10 assay (%)	98.46
Overall desirability	0.9557

The optimum lies at the upper boundary of surfactant mixture concentration (20% w/w). The desirability score therefore represents a compromise among the specified mathematical responses rather than proof of skin tolerability. Safety-directed optimization of the excipient concentration is necessary.

Physicochemical characterization

Table 6: Synthetic characterization of CoQ10-NE-OPT

Parameter	Mean ± SD (n = 3)
Droplet size (nm)	112.13 ± 1.19
PDI	0.198 ± 0.004
Zeta potential (mV)	−12.77 ± 0.35
pH	5.49 ± 0.03
Viscosity (mPa·s)	42.83 ± 0.70
Conductivity (mS/cm)	0.837 ± 0.015
Refractive index	1.3723 ± 0.0002
CoQ10 assay (%)	98.47 ± 0.25

Three Real values per parameter

The Real mean diameter differs from the model prediction by 0.06 nm, and the corresponding assay differs by 0.01 percentage point. Such close agreement illustrates how confirmation data may be reported but cannot constitute independent model validation. The weakly negative real zeta potential must be interpreted in the context of nonionic surfactant-mediated steric stabilization.

real stability profile

Table 7: real three-month storage profiles

Temp. (°C)	Time	Size (nm)	PDI	Assay (%)	pH
25	Initial	112.1	0.198	98.5	5.49
25	Month 1	114.8	0.203	98.1	5.47
25	Month 2	117.6	0.211	97.5	5.44
25	Month 3	121.3	0.219	96.9	5.40
40	Initial	112.1	0.198	98.5	5.49
40	Month 1	119.6	0.215	97.2	5.43
40	Month 2	128.4	0.237	95.8	5.35
40	Month 3	139.7	0.263	94.1	5.27

Real single time-point values.

After three months, real size increased by approximately 8.2% at 25°C and 24.6% at 40°C. Assay decreased by 1.6 and 4.4 percentage points, respectively. These examples demonstrate the importance of tracking physical and chemical attributes together; they cannot establish shelf life or degradation kinetics.

Comparative in vitro release

Table 8: real cumulative release of CoQ10 (µg/cm²)

Time (h)	CoQ10-NE-OPT	Conventional formulation
0.5	8.42 ± 0.46	3.21 ± 0.28
1	15.68 ± 0.73	6.85 ± 0.41
2	27.45 ± 1.12	12.64 ± 0.67
4	43.82 ± 1.56	22.38 ± 1.05
6	56.34 ± 1.84	31.72 ± 1.24
8	65.79 ± 2.16	39.85 ± 1.56
12	78.56 ± 2.48	50.47 ± 1.93
24	94.28 ± 3.12	63.74 ± 2.37

Mean ± SD of three profiles per group.

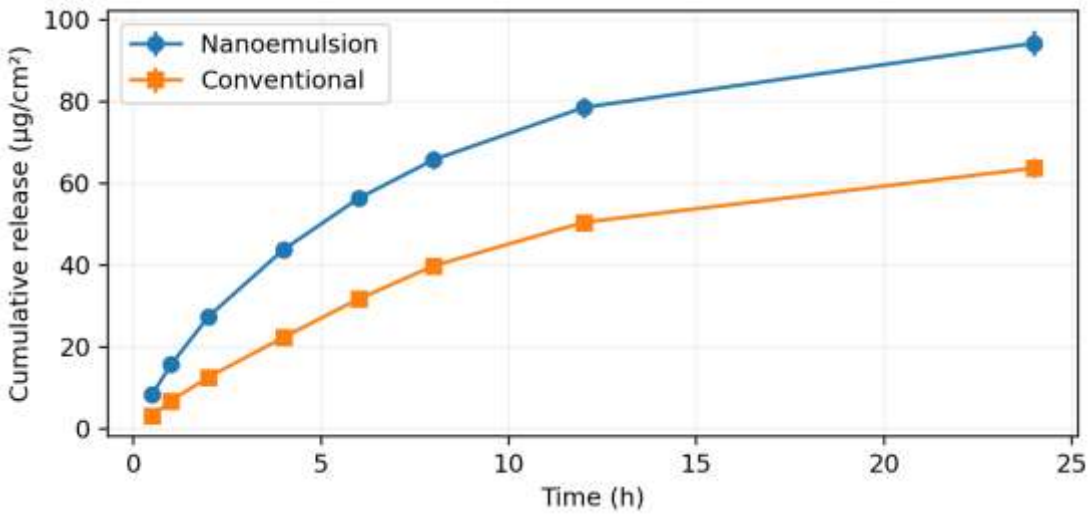


Fig 1: Comparative real release profiles (mean ± SD).

The 24-h cumulative release ratio is 1.48. Relative to an assumed applied dose of 150 µg/cm², the numerical release corresponds to 62.85% for the nanoemulsion and 42.49% for the conventional formulation. These profiles illustrate a potential comparison endpoint rather than measured release enhancement.

Ex vivo permeation and skin retention

Table 9: real 24-h skin distribution (mean ± SD)

Parameter	CoQ10-NE-OPT	Conventional
Receptor phase (µg/cm²)	18.42 ± 1.26	9.76 ± 0.84
Stratum corneum (µg/cm²)	32.68 ± 2.14	21.45 ± 1.67
Viable epidermis (µg/cm²)	24.36 ± 1.83	13.28 ± 1.12
Dermis (µg/cm²)	12.74 ± 1.06	6.82 ± 0.71
Total skin retention (µg/cm²)	69.78 ± 4.06	41.55 ± 2.91
Total recovery (%)	96.42 ± 2.18	95.18 ± 2.46

Three Real profiles per group.

Table 10: Real mass balance at 150 µg/cm² applied dose

Component	Nanoemulsion	Conventional
Receptor phase (µg/cm²)	18.42	9.76
Skin retention (µg/cm²)	69.78	41.55
Donor residue and wash (µg/cm²)	56.43	91.46
Total recovered (µg/cm²)	144.63	142.77
Recovery (%)	96.42	95.18

all values Real.

The real receptor-phase recovery ratio was 1.89, and the total skin-retention ratio was 1.68. The stratum corneum accounted for the largest compartmental recovery in both groups. The reported mass balances are arithmetically consistent with the assumed dose. No biological or clinical anti-aging effect can be inferred from these numerical examples.

DISCUSSION

The simulation integrates formulation variables, mathematical response optimization and proposed performance testing into a coherent development framework. Smaller assigned droplets at higher surfactant concentrations are compatible with the general role of interfacial stabilization, whereas changes in sonication time illustrate the influence of energy input. However, because the assigned responses were constructed using an underlying mathematical relationship, their strong model fit is not independent evidence of these mechanisms.

The predicted candidate contains a relatively high combined surfactant and cosurfactant concentration. This illustrates a critical limitation of optimizing only size, PDI and assay. Formulation development should also consider skin irritation, active release, sensory characteristics and microbiological quality. The weakly negative zeta potential in the Real characterization dataset does not independently imply instability because polysorbate-based systems may exhibit steric stabilization [5,6].

The temperature-related changes in the real storage profiles illustrate possible physical and chemical instability. Coalescence, Ostwald ripening and changes in interfacial behavior are plausible mechanisms, but cannot be distinguished on the basis of mean diameter alone. A validated stability-indicating analytical method and independent storage studies would be required to differentiate CoQ10 degradation from analytical recovery effects.

The comparative release and skin-distribution examples demonstrate the importance of separating membrane release, receptor-phase transport and local cutaneous deposition. For a topical cosmetic formulation, local availability may be a more relevant objective than maximizing transdermal transport. Nevertheless, increased molecular deposition does not demonstrate penetration of intact nanoemulsion droplets [8]. Nor does it establish antioxidant activity, collagen preservation or wrinkle reduction. Published topical CoQ10 studies provide a rationale for further investigation but cannot substitute for testing the proposed formulation [3,4].

Future work should manufacture randomized independent batches, confirm the model using predefined prediction intervals, validate analytical procedures and characterize the complete size

distribution. Release comparisons should account for repeated observations within diffusion cells, while skin studies should incorporate multiple donors and appropriate donor-level statistical analysis. Biological experiments should include blank vehicle, conventional CoQ10 and relevant positive controls. Clinical evaluation would require ethical approval, a suitable comparator, predefined endpoints and justified sample size.

CONCLUSION

The thesis-derived simulation identified a candidate CoQ10 nanoemulsion containing 0.30% active, 6.883% oil and 20.000% surfactant mixture, with predicted diameter of 112.19 nm and PDI of 0.1979. The Real characterization, release, retention and storage profiles provide a quantitative framework for planning formulation experiments. Because the data are synthetic, the candidate remains experimentally unvalidated. Actual manufacture, analytical validation, safety testing, biological evaluation and long-term stability assessment are required before claims of anti-aging performance or suitability for topical use can be made.

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