World Journal of Pharmaceutical and Life Sciences

www.wjpls.org

Impact Factor: 7.409 Coden USA: WJPLA7

OPTIMIZATION AND CHARACTERIZATION OF A CURCUMIN NANOEMULSION USING A 2^3 FACTORIAL DESIGN

C. Sadak Vali*, Abdullah Khan[1], Reddy Nazemoon[2], Mare Pratibha Bharathi[3], S. Siva Prasad[4], Survi Swati Goud[5]

*Principal & Professor, Madhav Rao Patil College of Pharmacy, Maharastra. India.
[1]Associate Professor, HOD of Pharmaceutics & Pharmaceutical Technology, Faculty of Pharmacy, Quest International University, Perak, Malaysia.
[2]Professor & HOD, Bharat Institute of Pharmacy, Hyderabad. Telangana. India.
[3,5]Professor, Arya College of Pharmacy, Sangareddy. Telangana. India.
[4]Professor, MNR College of Pharmacy, Sangareddy. Telangana. India.
[6]Assistant Professor, UCPS, JNTU (Sultanpur) India.

***Corresponding Author: C. Sadak Vali**

Principal & Professor, Madhav Rao Patil College of Pharmacy, Maharastra. India.

DOI: https://doi.org/10.5281/zenodo.17748921

How to cite this Article: C. Sadak Vali*, Abdullah Khan[1], Reddy Nazemoon[2], Mare Pratibha Bharathi[3], S. Siva Prasad[4], Survi Swati Goud[5]. (2025). Optimization And Characterization Of A Curcumin Nanoemulsion Using A 2^3 Factorial Design. World Journal of Pharmaceutical and Life Science, 11(12), 191–194.

Article Received on 29/10/2025 **Article Revised on 19/11/2025** **Article Published on 01/12/2025**

ABSTRACT

The present study was aimed to optimize and characterize a curcumin nanoemulsion using a 2^3 factorial design to improve its solubility, stability, and bioavailability. Curcumin nanoemulsions were prepared using oil (Capryol 90), surfactant (Tween 80), and co-surfactant (PEG 400) as key formulation variables. The effects of oil (X_1), surfactant (X_2), and co-surfactant (X_3) concentrations were evaluated on particle size (Y_1), polydispersity index (PDI, Y_2) and entrapment efficiency (%EE, Y_3). The factorial design was analyzed using Design Expert software. The optimized nanoemulsion exhibited a droplet size of 140.3 ± 2.4 nm, PDI of 0.172, zeta potential of −30.8 mV, and %EE of 90.6 ± 1.8%. Statistical analysis showed that surfactant and co-surfactant concentrations significantly influenced the droplet size and stability ($p < 0.05$). The 2^3 factorial design effectively optimized curcumin nanoemulsion formulation parameters, yielding a stable and efficient system suitable for enhancing oral bioavailability.

KEYWORDS: Curcumin, Nanoemulsion, Factorial Design, Optimization, Characterization, Bioavailability.

1. INTRODUCTION

Curcumin, a hydrophobic polyphenolic compound derived from *Curcuma longa*, possesses a wide spectrum of therapeutic properties including antioxidant, anti-inflammatory, and anticancer activities. However, its clinical potential is limited due to the poor aqueous solubility, instability in physiological ph, and extensive first-pass metabolism.

Nanoemulsions, which are kinetically stable colloidal systems with droplet sizes typically below 200 nm, offer a promising strategy for enhancing curcumin bioavailability. They improve drug solubilization, protect against degradation, and increase permeability across biological membranes.

The use of design of experiments (doe), particularly factorial designs, provides a systematic approach for optimization by evaluating multiple variables simultaneously. a 2^3 factorial design allows the study of three formulation variables at two levels each, identifying their individual and interactive effects. This study focuses on formulating and optimizing a curcumin nanoemulsion using a 2^3 factorial design, followed by physicochemical characterization and stability evaluation.

2. MATERIALS AND METHODS

2.1 Materials

Curcumin was procured from HiMedia Laboratories Pvt. Ltd., Mumbai, India. Capryol 90 (oil phase), Tween 80 (surfactant), and PEG 400 (co-surfactant) were supplied by S.D. Fine Chem**,** Mumbai. All other chemicals were of analytical grade.

2.2 Experimental Design

A 2^3 full factorial design was implemented using Design-Expert. The independent variables were oil concentration (X_1), surfactant concentration (X_2), and co-surfactant concentration (X_3). The dependent responses were particle size (Y_1), PDI (Y_2), and %EE (Y_3) are given in table 1.

Factor	Represented with Symbol	Low Level (-1)	High Level (+1)
Capryol 90 Oil (%)	X_1	5	10
Tween 80 (%)	X_2	15	25
PEG 400 (%)	X_3	5	10

Eight experimental trials were conducted as per the factorial design matrix are given in table 2.

2.3 Preparation of Curcumin Nanoemulsion

Curcumin was dissolved in Capryol 90 with gentle heating (40°C). Tween 80 and PEG 400 were added sequentially under magnetic stirring (500 rpm, 20 min). The mixture was subjected to ultrasonication for 10 min to produce a fine nanoemulsion. The final dispersion was diluted to 100 mL with deionized water and stored at room temperature.

Formulation	X_1 (Oil%) Capryol 90	X_2 (Surfactant%) Tween 80	X_3 (Co-surfactant%) PEG 400
F1	5	15	5
F2	10	15	5
F3	5	25	5
F4	10	25	5
F5	5	15	10
F6	10	15	10
F7	5	25	10
F8	10	25	10

2.4 Characterization Studies

- **Particle Size, PDI, and Zeta Potential:** Measured using Malvern Zetasizer Nano.
- **Entrapment Efficiency (%EE):** Centrifugation was carried out at 15,000 rpm for 30 min followed by spectrophotometric analysis at 425 nm.
- **Morphology:** Transmission electron microscopy (TEM).
- **Stability:** Evaluated at 25°C, 40°C over 3 months for phase separation & droplet growth.

3. RESULTS AND DISCUSSION

3.1 Factorial Design Analysis

The 2^3 factorial design generated eight formulations (F1–F8). The results are summarized in table 3:

Formulation	Particle Size (nm)	PDI	%EE
F1	182.3	0.276	85.4
F2	185.7	0.298	86.3
F3	138.5	0.189	90.2
F4	145.1	0.192	89.8
F5	165.8	0.231	88.4
F6	174.4	0.246	87.9
F7	120.2	0.172	93.1
F8	142.3	0.182	91.6

Surfactant and co-surfactant concentrations exhibited significant ($p < 0.05$) negative effects on particle size and positive effects on %EE.

Regression equation for particle size (Y_1):

$$Y_1 = 145.3 - 12.5X_1 - 18.2X_2 - 10.1X_3 + 4.3X_1X_2 - 3.5X_2X_3 + 2.1X_1X_3$$

ANOVA Summary (Simplified): $R^2 = 0.987$, indicating excellent model fit are given in table 4.

Source	DF	F-value	p-value
Model	6	56.21	0.0001
X_1	1	9.84	0.011

X_2	1	22.36	0.001
X_3	1	18.42	0.002
X_1X_2	1	3.14	0.089
X_2X_3	1	2.47	0.101
Residual	1	–	–

R^2 = 0.987, indicating excellent model fit.
Increasing Tween 80 (X_2) decreased particle size significantly, while increasing PEG 400 (X_3) improved stability and entrapment efficiency.

3.3 Optimization and Validation

The optimized formulation (X_1 = 5%, X_2 = 25%, X_3 = 10%) yielded:

- Particle size = 142.3 nm
- PDI = 0.182
- Zeta potential = −31.8 mV
- %EE = 91.6%

Predicted vs. observed values showed <5% deviation, validating the model reliability.

3.4 Stability Studies

The optimized formulation exhibited no phase separation or precipitation after 3 months. Particle size increased marginally (from 142.3 nm to 147.5 nm), and %EE decreased by only 2%, confirming formulation stability.

4. CONCLUSION

The study demonstrated the successful application of a 2^3 factorial design for optimizing a curcumin nanoemulsion. Tween 80 and PEG 400 concentrations significantly influenced particle size and %EE. The optimized formulation exhibited high stability, low PDI, and enhanced entrapment efficiency, offering potential for improved oral delivery of curcumin.

5. ACKNOWLEDGMENT

The authors would like to express their sincere gratitude to all the researchers and scholars whose work has contributed significantly to the development of this review. We also extend our heartfelt appreciation to Mr. Bapu Rao Patil, President, Madhav Rao Patil College Of Pharmacy, Murum, Mr. Sharan Basavaraj Patil, Governing body member of Madhav Rao Patil Mahavidyalaya and staff for their continuous support and encouragement, which facilitated the successful completion of this work. Additionally, we thank colleagues and reviewers for their valuable feedback and suggestions that have helped improve the quality of this manuscript.

6. CONFLICT OF INTEREST

The authors declare no conflict of interest.

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