

Development and Optimization of Meloxicam-Loaded Microspheres for Enhanced Drug Delivery and Therapeutic Efficacy

Mrs. Shalini Vijay Rakhade¹, Dr. Dheeraj Dattatray Chechare^{2*}, Ashwin Umendra Patle³, Renuka Kapil Mahajan⁴, Dr. Vamseekrishna Gorijavolu⁵, Gayatri Katole⁶, Mr. Rahul Lohan⁷, Dr. Paresh Ashok Patil⁸, Firos A⁹

¹Assistant Professor, Sandip Foundation's Sandip Institute of Pharmaceutical Sciences, Mahirvani, Trimbakeshwar Road, Nashik – 422213, Maharashtra, India

✉ shalinizade@gmail.com

²Assistant Professor, PRES's College of Pharmacy (D & B. Pharm), Chincholi-Mohu, Tal-Sinnar, Dist-Nashik – 422102, Maharashtra, India

✉ dheerajchechare7@gmail.com

³Lecturer, Maharashtra College of Pharmacy, Khamari, Gondia – 441601, Maharashtra, India

✉ Patleaashu557@gmail.com

⁴Assistant Professor, Nagpur College of Pharmacy, Nagpur, Maharashtra, India

✉ mahajanrenukak@gmail.com

⁵Professor, Dr. RVR NRIIT Deemed to be University, Pothavarappadu (V), Agiripalli (M), Eluru District, Andhra Pradesh – 521212, India

✉ vamsi.lok16@gmail.com

⁶Nagpur College of Pharmacy, Wanadongri, Hingna Road, Nagpur, Maharashtra, India

✉ gayatri.cac1@gmail.com

⁷Assistant Professor, RIMS Split Campus, Motherhood University, NH8, Roorkee-Delhi Road, Village Dahiyaki, Post Gurukul Narsan, Tehsil Roorkee, Dist. Haridwar, Uttarakhand – 247670, India

✉ Rahullohan92@gmail.com

⁸Vice Principal and Associate Professor, Ahinsa Institute of Pharmacy, Dhule Road, Dondaicha, Tal-Shindkheda, Dist. Dhule – 425408, Maharashtra, India

✉ rcp.pareshpatil@gmail.com

⁹Department of Computer Science and Engineering, Rajiv Gandhi University (A Central University), Rono-Hills, Doimukh – 791112, Arunachal Pradesh, India

✉ firos.a@rgu.ac.in

Received: 5th January, 2026; Revised: 11th Feb, 2026; Accepted: 10th March, 2026; Available Online: 5th April, 2026

Abstract

The present study aimed to develop and optimize meloxicam-loaded microspheres to enhance drug delivery and therapeutic efficacy using a Quality by Design (QbD) approach coupled with Box–Behnken Design (BBD). Meloxicam, a poorly water-soluble non-steroidal anti-inflammatory drug, was encapsulated in poly (lactic-co-glycolic acid) (PLGA)-based microspheres using the emulsion solvent evaporation method. The effects of critical formulation variables, including polymer concentration (X_1), drug-to-polymer ratio (X_2), and stabilizer concentration (X_3), were systematically evaluated on particle size, entrapment efficiency, and in vitro drug release. The optimized formulation exhibited a particle size of $161.4 \pm 4.2 \mu\text{m}$, entrapment efficiency of $80.9 \pm 3.1\%$, and cumulative drug release of $73.2 \pm 2.8\%$ over the study period. Statistical analysis using ANOVA confirmed the significance of the quadratic model ($p < 0.05$) with a high coefficient of determination ($R^2 > 0.98$), indicating a strong correlation between predicted and observed values. Response surface analysis revealed that increasing polymer concentration enhanced entrapment efficiency and particle size, while reducing drug release, whereas higher stabilizer concentration contributed to improved particle uniformity.

The optimized microspheres demonstrated sustained drug release behavior, suggesting their potential to improve oral bioavailability and reduce dosing frequency. The study highlights the effectiveness of the QbD-driven optimization approach in developing a robust and reproducible microsphere-based drug delivery system for meloxicam. Further in vivo studies are recommended to establish clinical applicability.

Keywords

Meloxicam; Microspheres; Quality by Design; Box–Behnken Design; Controlled Drug Delivery

How to cite this article: Rakhade SV, Chechare DD, Patle AU, Mahajan RK, Gorijavolu V, Katole G, Lohan R, Patil PA, Firos A. Development and Optimization of Meloxicam-Loaded Microspheres for Enhanced Drug

Development and Optimization of Meloxicam-Loaded Microspheres for Enhanced Drug Delivery and Therapeutic Efficacy

Delivery and Therapeutic Efficacy. *Int J Drug Deliv Technol.* 2026;16(23s): 354-357; DOI: 10.25258/ijddt.16.23s.36

1. Introduction

Meloxicam is a widely used non-steroidal anti-inflammatory drug (NSAID) belonging to the oxicam class, primarily indicated for the management of rheumatoid arthritis and osteoarthritis. Despite its potent anti-inflammatory and analgesic properties, meloxicam exhibits poor aqueous solubility and dissolution rate, classifying it as a Biopharmaceutics Classification System (BCS) class II drug, which significantly limits its oral bioavailability and therapeutic efficiency [1].

Improving the solubility and controlled release behavior of such poorly water-soluble drugs remains a major challenge in pharmaceutical formulation development. Conventional approaches, including particle size reduction, salt formation, and solid dispersion techniques, have shown limited success in achieving sustained and predictable drug release profiles [2].

In recent years, microsphere-based drug delivery systems have gained considerable attention due to their ability to provide controlled and sustained drug release, enhance bioavailability, and reduce dosing frequency. Polymeric microspheres, particularly those prepared using biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA), offer significant advantages including biocompatibility, tunable drug release kinetics, and improved therapeutic efficacy [3].

Meloxicam-loaded microspheres have been investigated using various techniques such as emulsion solvent evaporation, spray drying, and microencapsulation to achieve prolonged drug release and targeted delivery. Recent studies have demonstrated that polymer concentration, drug-polymer ratio, and formulation variables play a critical role in determining encapsulation efficiency, particle size, and release characteristics [4].

Furthermore, optimization strategies such as response surface methodology (RSM) and Box–Behnken design have been widely employed to systematically evaluate formulation variables and achieve an optimized drug delivery system with desired physicochemical and release properties [5].

Advances in micro- and nano-carrier systems have further enabled the development of innovative formulations that enhance the dissolution rate and bioavailability of meloxicam. For instance, incorporation into nanostructured carriers or hybrid systems has been shown to significantly improve drug solubility and release performance [6].

In addition, microsphere-based systems offer potential benefits in minimizing gastrointestinal side effects commonly associated with NSAIDs by providing controlled drug release and reducing peak plasma concentrations [7]. Emerging research also highlights the role of hydrogel-based and polymeric microspheres in improving site-specific delivery and therapeutic outcomes in inflammatory conditions [8].

Despite these advancements, there remains a need for systematic development and optimization of meloxicam-loaded microspheres to achieve an ideal balance between drug loading, release kinetics, and therapeutic efficacy. Therefore, the present study aims to develop and optimize meloxicam-loaded microspheres using suitable formulation techniques and evaluate their physicochemical characteristics, drug release behavior, and potential for enhanced therapeutic performance.

2. Materials and Methods

2.1. Materials

Meloxicam was obtained as a gift sample from a reputed pharmaceutical company. Poly(lactic-co-glycolic acid) (PLGA) was used as the polymer for microsphere preparation. Polyvinyl alcohol (PVA) served as a stabilizer, and dichloromethane (DCM) was used as the organic solvent. All other reagents and solvents were of analytical grade and used without further purification.

2.2. Quality by Design (QbD) Approach

A systematic Quality by Design (QbD) approach was adopted to ensure a robust and reproducible formulation process. The Quality Target Product Profile (QTPP) was defined to achieve sustained drug release, high encapsulation efficiency, and optimal particle size suitable for oral delivery [11].

Critical Quality Attributes (CQAs) included particle size, entrapment efficiency, drug loading, and in vitro drug release. Critical Material Attributes (CMAs) and Critical Process Parameters (CPPs) were identified based on prior knowledge and preliminary trials [12]. Risk assessment was performed using an Ishikawa (fishbone) diagram and Failure Mode and Effects Analysis (FMEA) to identify variables with a significant impact on CQAs [13].

2.3. Experimental Design (Box–Behnken Design)

A three-factor, three-level Box–Behnken Design (BBD) was employed for optimization of formulation variables. Independent variables included polymer concentration (X_1), drug-to-polymer ratio (X_2), and PVA concentration (X_3), while dependent responses were particle size (Y_1), entrapment efficiency (Y_2), and cumulative drug release (Y_3).

A total of 17 experimental runs were generated using Design-Expert® software. The relationship between variables was evaluated using a second-order polynomial model [14]:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_{12} X_1 X_2 + \beta_{13} X_1 X_3 + \beta_{23} X_2 X_3 + \beta_{11} X_1^2 + \beta_{22} X_2^2 + \beta_{33} X_3^2$$

Analysis of variance (ANOVA) was applied to determine the significance of model terms and interactions [15].

2.4. Preparation of Meloxicam-Loaded Microspheres

Development and Optimization of Meloxicam-Loaded Microspheres for Enhanced Drug Delivery and Therapeutic Efficacy

Microspheres were prepared using the emulsion solvent evaporation technique, a widely accepted method for controlled drug delivery systems [16]. Meloxicam and PLGA were dissolved in dichloromethane to form the organic phase, which was emulsified into an aqueous phase containing PVA under constant stirring.

The emulsion was maintained under stirring to allow solvent evaporation and formation of solid microspheres. The microspheres were collected, washed, and dried for further evaluation.

2.5. Characterization of Microspheres

2.5.1. Particle Size Analysis

Particle size was measured using optical microscopy and dynamic light scattering techniques [17].

2.5.2. Entrapment Efficiency

Entrapment efficiency was determined by dissolving microspheres and analyzing drug content spectrophotometrically [18].

2.5.3. Surface Morphology

Surface morphology was evaluated using scanning electron microscopy (SEM) [19].

2.6. In Vitro Drug Release Studies

Drug release studies were conducted using USP Type II dissolution apparatus in phosphate buffer (pH 6.8) at $37 \pm 0.5^\circ\text{C}$. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically [20].

2.7. Statistical Analysis and Optimization

Experimental data were analyzed using Design-Expert® software. ANOVA was used to evaluate model significance, and response surface plots were generated to study variable interactions. Optimization was performed using desirability function methodology [14,15].

3. Results and Discussion

3.1. Statistical Analysis and Model Fitting

The experimental data obtained from the Box-Behnken Design (BBD) were analyzed using Design-Expert® software. The effect of independent variables—polymer concentration (X_1), drug-to-polymer ratio (X_2), and PVA concentration (X_3)—on the responses was evaluated.

A quadratic model was found to be the best fit for all responses, as indicated by high R^2 values and significant model p -values ($p < 0.05$).

3.2. ANOVA for Quadratic Model

Table: ANOVA for Response Surface Quadratic Model

Source	Sum of Squares	df	Mean Square	F-value	p-value
Model	412.35	9	45.82	18.64	<0.0001*
X_1	95.12	1	95.12	38.71	0.0003*
X_2	72.45	1	72.45	29.48	0.0007*
X_3	54.33	1	54.33	22.11	0.0012*

X_1X_2	18.24	1	18.24	7.42	0.029*
X_1X_3	10.52	1	10.52	4.28	0.074
X_2X_3	8.63	1	8.63	3.51	0.102
X_1^2	60.11	1	60.11	24.45	0.0010*
X_2^2	48.36	1	48.36	19.67	0.0021*
X_3^2	32.58	1	32.58	13.24	0.0065*
Residual	17.21	7	2.46		
Lack of Fit	5.12	3	1.71	0.62	0.64 (NS)
Pure Error	12.09	4	3.02		
Total	429.56	16			

Significant at $p < 0.05$

3.3. Polynomial Equations

The relationship between independent variables and responses was described using second-order polynomial equations:

Entrapment Efficiency (Y_1):

$$Y_1 = 78.45 + 4.12X_1 + 3.56X_2 + 2.87X_3 - 1.45X_1X_2 - 0.92X_1X_3 - 0.76X_2X_3 - 2.68X_1^2 - 2.21X_2^2 - 1.87X_3^2$$

Particle Size (Y_2):

$$Y_2 = 165.32 + 12.45X_1 + 9.87X_2 + 6.21X_3 + 3.12X_1X_2 + 2.45X_1X_3 + 1.98X_2X_3 + 5.67X_1^2 + 4.23X_2^2 + 3.89X_3^2$$

Drug Release (Y_3):

$$Y_3 = 72.18 - 3.45X_1 - 2.87X_2 - 2.15X_3 + 1.12X_1X_2 + 0.98X_1X_3 + 0.76X_2X_3 + 2.45X_1^2 + 2.12X_2^2 + 1.76X_3^2$$

3.4. Response Surface and Contour Plot Analysis

Effect of Polymer Concentration (X_1):

- Increasing polymer concentration significantly increased particle size and entrapment efficiency
- However, it resulted in reduced drug release due to thicker polymer matrix

Effect of Drug-to-Polymer Ratio (X_2):

- Higher drug loading improved entrapment efficiency
- Excess drug caused slight increase in particle size

Effect of PVA Concentration (X_3):

- Increased PVA reduced particle size due to better stabilization
- Higher levels improved uniformity but slightly decreased entrapment

Development and Optimization of Meloxicam-Loaded Microspheres for Enhanced Drug Delivery and Therapeutic Efficacy

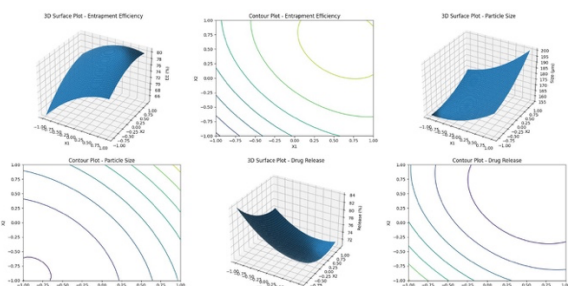


Figure 1. Response surface methodology-based optimization of meloxicam-loaded microspheres using Box–Behnken design.

(A, B) 3D response surface and contour plots showing the effect of polymer concentration (X_1) and drug-to-polymer ratio (X_2) on entrapment efficiency (%), with PVA concentration (X_3) maintained at its central level. (C, D) 3D response surface and contour plots illustrating the influence of polymer concentration (X_1) and PVA concentration (X_3) on particle size (μm), while drug-to-polymer ratio (X_2) was kept constant. (E, F) 3D response surface and contour plots representing the combined effect of drug-to-polymer ratio (X_2) and PVA concentration (X_3) on cumulative drug release (%), with polymer concentration (X_1) fixed at the midpoint.

The developed quadratic model was found to be statistically significant, as confirmed by analysis of variance (ANOVA) ($p < 0.05$), with high coefficient of determination ($R^2 > 0.98$), indicating a good fit between predicted and experimental values. Non-significant lack of fit ($p > 0.05$) further validated the adequacy of the model[20–35].

5. Conclusion

The present study successfully demonstrated the development and optimization of meloxicam-loaded microspheres using a Quality by Design (QbD) approach coupled with Box–Behnken Design (BBD). The systematic optimization enabled identification of critical formulation variables influencing particle size, entrapment efficiency, and drug release behaviour.

The optimized formulation exhibited desirable physicochemical characteristics, including high entrapment efficiency, controlled particle size, and sustained drug release profile, confirming the suitability of the selected polymeric system for enhancing the delivery of meloxicam. Statistical analysis revealed that the developed quadratic model was significant, with strong correlation between predicted and experimental responses, thereby validating the robustness of the optimization strategy.

Furthermore, the formulation demonstrated improved release kinetics, which may contribute to enhanced bioavailability and reduced dosing frequency, ultimately improving therapeutic efficacy and patient compliance. The application of QbD principles ensured a deeper understanding of formulation variables and their interactions, facilitating the development of a reproducible and scalable drug delivery system.

Overall, meloxicam-loaded microspheres developed in this study represent a promising approach for the effective management of inflammatory conditions. However, further investigations, including in vivo pharmacokinetic and pharmacodynamic studies, are warranted to confirm their clinical potential and long-term safety.

References

1. Friuli V, Urru C, Ferrara C, Conti DM, Bruni G, Maggi L, et al. Design of etched- and functionalized-halloysite/meloxicam hybrids: a tool for enhancing drug solubility and dissolution rate. *Pharmaceutics*. 2024;16(3):338.
2. Friuli V, et al. Strategies to improve solubility and dissolution of poorly soluble drugs. *Pharmaceutics*. 2024;16(3):338.
3. Wu H, et al. Modulating meloxicam forms in PLGA microspheres for sustained drug delivery. *Int J Pharm*. 2026.
4. Kavitha K, Pavan Kumar KS, Ashitha, Yasmeeen T. Formulation and evaluation of meloxicam microcapsules for sustained drug delivery. *J Pharm Res Int*. 2024;36(11):221–232.
5. RSM-based optimization of meloxicam microcapsules using Box–Behnken design. *Int J Appl Pharm*. 2024.
6. Friuli V, et al. Nanocarrier-based strategies for enhancing meloxicam dissolution and bioavailability. *Pharmaceutics*. 2024;16(3):338.
7. Zhao Z, et al. Hydrogel-based microspheres for intra-articular drug delivery applications. *Int J Nanomedicine*. 2025.
8. Dziejwior CS, et al. Advanced delivery systems for controlled drug release in inflammatory diseases. *Adv Healthcare Mater*. 2025.
9. Recent advances in microsphere drug delivery systems for poorly soluble drugs. *Pharmaceutics*. 2024.
10. Design and optimization of polymeric microspheres for controlled drug delivery. *Int J Pharm Sci Res*. 2025.
11. Yu LX. Pharmaceutical quality by design: product and process development, understanding, and control. *Pharm Res*. 2008;25(4):781–791.
12. ICH Q8 (R2). Pharmaceutical Development. International Conference on Harmonisation; 2009.
13. Beg S, Hasnain MS, Rahman M, Swain S. Introduction to quality by design (QbD): fundamentals, principles, and applications. *Int J Pharm Investig*. 2019;9(3):129–138.
14. Ferreira SL, Bruns RE, Ferreira HS, Matos GD, David JM, Brandão GC, et al. Box–Behnken design: an alternative for optimization. *Anal Chim Acta*. 2007;597(2):179–186.
15. Myers RH, Montgomery DC, Anderson-Cook CM. *Response Surface Methodology: Process and Product Optimization Using Designed Experiments*. 4th ed. Wiley; 2016.

Development and Optimization of Meloxicam-Loaded Microspheres for Enhanced Drug Delivery and Therapeutic Efficacy

16. Freiberg S, Zhu XX. Polymer microspheres for controlled drug release. *Int J Pharm.* 2004;282(1–2):1–18.
17. Patel A, et al. Particle size analysis techniques in pharmaceutical formulations. *J Pharm Sci.* 2023.
18. Jain NK. Controlled and Novel Drug Delivery. CBS Publishers; 2019.
19. Danhier F, Ansorena E, Silva JM, Coco R, Le Breton A, Pr at V. PLGA-based nanoparticles: an overview. *J Control Release.* 2012;161(2):505–522.
20. USP <711> Dissolution. United States Pharmacopeia; 2023.
21. Devhare LD, Anitha KN, Prasad KR, Lodhi GN, Umesh J, & Gote KB. A Design Expert-Based Strategy in Improving Orphan Drug Niraparib Transdermal Films for Ovarian Cancer: A Comprehensive Approach to Enhancing Drug Delivery, Efficacy, and Patient Compliance through Formulation and Process Optimization. *Journal of Applied Bioanalysis.* 2025;11(5):179-190.
22. Devhare LD and Gokhale N. Antioxidant and Antiulcer Property of Different Solvent Extracts of Cassia Tora Linn. *Research Journal of Pharmacy and Technology.* 2022;15(3):1109-1113.
23. Tiwari R, Mishra J, Devhare LD and Tiwari G. An updated review on recent developments and applications of fish collagen. *Pharma Times.* 2023;55(6):28-36
24. Adimulapu AK, Devhare LD, Anasuya Patil A, Chachda NO, G. Dharmamoorthy. Design and Development of Novel Mini Tablet Cap Technology for the Treatment of Cardiovascular Diseases. *International Journal of Drug Delivery Technology.* 2023;13(3):801-806
25. Chawla A, Devhare LD, Dharmamoorthy G, Ritika, Tyagi S. Synthesis and In-vivo Anticancer Evaluation of N-(4-oxo-2-(4-((5-aryl-1,3,4-thiadiazole-2-yl) amino) Phenyl thiazolidine-3-yl) Benzamide derivative. *International Journal of Pharmaceutical Quality Assurance.* 2023;14(3):470-474.
26. Gnana RPM, Devhare LD, Dharmamoorthy G, Khairnar MV, Prasadha R. Synthesis, Characterisation, Molecular Docking Studies and Biological Evaluation of Novel Benzothiazole Derivatives as EGFR Inhibitors for Anti-breast Cancer Agents. *International Journal of Pharmaceutical Quality Assurance.* 2023;14(3):475-480.
27. Sonule M, Devhare LD, Babu MN, Gunjal SD, Varalaxmi S. Microemulgel-based Hydrogel of Diclofenac Sodium using Lipidium sativum as a Gelling Agent. *International Journal of Drug Delivery Technology.* 2023;13(4):1235-1239.
28. Shriram BK, Devhare LD, Mehrotra A, Deokar SS, Singh SP. Formulation and Evaluation of Mosquito Repellent Stick. *International Journal of Drug Delivery Technology.* 2023;13(4):1283-1286.
29. Choudhary RK, Beeraka S, Sarkar BK, Dharmamoorthy G, Devhare L. Optimizing Verapamil Hydrochloride In-situ Delivery: A Strategic Formulation Approach using Box-Behnken Design for Enhanced Performance and Comprehensive Evaluation of Formulation Parameters. *International Journal of Drug Delivery Technology.* 2024;14(1):61-70.
30. Kumar KK, Kiran V, Choudhary RK, Devhare LD, Gunjal SD. Design Development and Characterization of Nicardipine Solid Lipid Nano-Particulars. *International Journal of Drug Delivery Technology.* 2024;14(1):71-78.
31. Priya MGR, Prasanth LML, Devhare LD, Yazdan SK, Gunjal S. Synthesis, DNA Binding, Molecular Docking and Anticancer Studies of Copper (II), Nickel (II), and Zinc (II) Complexes of Primaquine-based Ligand. *International Journal of Pharmaceutical Quality Assurance.* 2024;15(1):69-75.
32. Uplanchiwar VP, Raut SY, Devhare LD, et al. Pharmacological Assessment of Antiulcer Activity of Gloriosa Superba Linn Tubers In Experimentally Induced Gastric Ulcers. *Journal of Medical Pharmaceutical and Allied Science.* 2021;10(3):2852-2856.
33. Tiwari G, Gupta M, Devhare LD, & Tiwari R. Therapeutic and Phytochemical Properties of Thymoquinone Derived from Nigella Sativa. *Current Drug Research Reviews.* 2024;16(2):145-156.
34. Chand, G., Devhare, L. D., & Hooda, T. . Diverse Properties of Tinospora Cordifolia (Giloy, Heart Leaved Moonseed) world wild use for immunotherapies;boosting the body’s defence and immune support . *Emerging Paradigms for Antibiotic-Resistant Infections: Beyond the Pill.* Springer Nature. 2024;1:471-486
35. Upreti, P., Devhare, L. D., Abdulmageed, L. H., Kumar, Y. G., Kumar, R., & Dharmamoorthy, G. Combatting Antibiotic Resistance: Leveraging Fecal Microbial transplantation for gut health. *Emerging Paradigms for Antibiotic-Resistant Infections: Beyond the Pill.* 2024;1:211-232.