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Drug Delivery Letters, XXXX, XX, 1-18

RESEARCH ARTICLE

A Systematic Quality by Design-Based Formulation Study to Develop Optimized Ciprofloxacin Hydrochloride-Loaded Nanoparticles for Controlled Drug Release

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Abstract: ***Introduction*:** Nanoparticles have been developed to enhance the delivery of Ciprofloxacin hydrochloride, improve therapeutic efficacy, and address the challenges of conventional antibiotic therapy, including biofilm penetration and drug resistance. The study aimed to optimize Ciprofloxacin hydrochloride-loaded nanoparticles using Face-Centered Central Composite Design (FCCCD) within a Quality by Design (QbD) framework, focusing on critical quality attributes (CQA) and critical material attributes (CMA).

***Methods*:** Thirteen experimental batches were prepared using FCCCD with ethyl cellulose (EC) and Tween 80 as independent variables. The formulations were characterized in terms of encapsulation efficiency, particle size, and drug release. Optimization was performed using Design Expert software (Stat-Ease 360 trial version) with response surface methodology. The optimized formulation was validated through four checkpoint batches. Similarity factor analysis and accelerated stability studies were conducted in accordance with ICH guidelines.

***Results*:** The optimized formulation demonstrated an encapsulation efficiency of 74.66 ± 1.01%, a particle size of 83.64 ± 0.23 nm, and a drug release of 77.70 ± 0.53%. Statistical analysis confirmed the significance of the response models ($p < 0.05$) with high R^2 values (0.9930 for encapsulation efficiency, 0.9880 for particle size, and 0.9963 for drug release), validating the predictive capability of the model. The experimental checkpoint batches showed strong agreement between predicted and observed values. Similarity factor analysis ($f2 = 60$) indicated a close match between the drug release profile of the optimized and reference formulations. Stability studies confirmed the physical and chemical stability of the product over three months.

***Discussion*:** FCCCD effectively optimized Ciprofloxacin hydrochloride nanoparticles by systematically evaluating the impact of EC and Tween 80 on CQA. The use of response surface methodology ensured resource efficiency while identifying an optimal formulation space. The similarity in release profile with the reference formulation and the confirmed stability highlight the clinical relevance of the optimized nanoparticles.

***Conclusion*:** The study demonstrated that FCCCD is a robust and resource-efficient statistical tool for nanoparticle optimization. Ciprofloxacin hydrochloride nanoparticles with high encapsulation efficiency, controlled release, and confirmed stability were successfully developed, offering a cost-effective approach for improved antibiotic delivery.

ARTICLE HISTORY

Received: May 03, 2025
Revised: August 05, 2025
Accepted: August 22, 2025

DOI:
10.2174/0122103031403695251117184720

Keywords: Critical quality attributes, ethyl cellulose, face centered central composite design, quality by design, similarity factor, tween 80, validation check.

1. INTRODUCTION

Face-Centered Central Composite Design (FCCCD) is a widely used experimental design technique for optimizing formulations with minimal effort. It is specifically used for constructing a quadratic model to optimize processes in which multiple variables may affect the dependent response of interest [1]. FCCCD is used to determine the impact of independent input factors and their combined effects on one or more dependent factors [2]. The Response Surface Methodology (RSM) approach is used in optimizing studies to understand the impact of independent variables on the dependent response. A quadratic model was fitted to the exper-

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