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**Research Article**

# Nanotechnology-Based Delivery Systems for Enhancing the Bioavailability of Quercetin: *In-Vitro* study analysis

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ABSTRACT

This study aimed to develop and characterize quercetin-loaded nanoparticles to enhance the bioavailability of quercetin through nanotechnology-based delivery systems. The nanoparticles were prepared and evaluated for their physicochemical properties, encapsulation efficiency, and in vitro drug release profile. Dynamic light scattering (DLS) analysis revealed an average particle size of 162.4 ± 5.3 nm, with a polydispersity index (PDI) of 0.192 ± 0.02, indicating a monodisperse system. The zeta potential was measured at -32.7 ± 2.4 mV, confirming excellent colloidal stability due to strong electrostatic repulsion. Scanning electron microscopy (SEM) images demonstrated uniform, spherical nanoparticles with consistent morphology. The encapsulation efficiency (EE) and loading capacity (LC) were calculated to be 85.2% and 12.5%, respectively, highlighting the system's ability to effectively encapsulate and retain quercetin. In vitro drug release studies exhibited a sustained release profile, with an initial burst release within the first 2 hours followed by gradual release over 72 hours, achieving 85% cumulative release.

**Keywords**: Quercetin, Nanoparticles, Bioavailability, Drug Delivery, Sustained Release

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## 1. INTRODUCTION

Quercetin, a naturally occurring flavonoid found in fruits, vegetables, and medicinal plants, has garnered significant attention due to its wide range of biological activities, including antioxidant, anti-inflammatory, anticancer, and cardioprotective effects [1, 2]. Despite its promising therapeutic potential, the clinical application of quercetin is limited by its poor bioavailability, which is attributed to its low aqueous solubility, instability in physiological conditions, and extensive first-pass metabolism [3, 4]. These challenges have prompted researchers to explore innovative strategies to enhance the delivery and efficacy of quercetin.

Nanotechnology has emerged as a powerful tool in the field of drug delivery, offering unique advantages such as improved solubility, controlled release, and targeted delivery of bioactive compounds [5, 6]. Nanocarriers, including liposomes, polymeric nanoparticles, solid lipid nanoparticles (SLNs), and nanoemulsions, have been extensively investigated for their ability to enhance the bioavailability and therapeutic efficacy of poorly soluble drugs [7]. By encapsulating quercetin within nanocarriers, it is possible to protect it from degradation, improve its absorption, and achieve sustained release, thereby maximizing its therapeutic potential [8].

Recent studies have demonstrated the feasibility of using nanotechnology-based delivery systems for quercetin. For instance, polymeric nanoparticles have been shown to enhance the oral bioavailability of quercetin by facilitating its absorption in the gastrointestinal tract [9]. Similarly, lipid-based nanocarriers have been reported to improve the stability and bioavailability of quercetin, making it a promising candidate for various therapeutic applications [10]. However, there is a need for comprehensive in vitro and in vivo studies to evaluate the efficacy, safety, and pharmacokinetic profile of these delivery systems.

This study aims to develop and characterize nanotechnology-based delivery systems for quercetin and evaluate their potential to enhance its bioavailability. The in vitro studies will focus on the physicochemical properties, drug release kinetics, and cellular uptake of the nanocarriers, while the in vivo studies will assess the pharmacokinetic profile and therapeutic efficacy of quercetin-loaded nanoparticles. The findings of this research will provide valuable insights into the application of nanotechnology for improving the delivery of quercetin and other poorly soluble bioactive compounds, paving the way for their use in clinical and industrial settings.

## 2. Materials and Methods

### *2.1 Materials*

Quercetin (purity ≥ 95%) was purchased from Sigma-Aldrich (St. Louis, MO, USA). Poly(lactic-co-glycolic acid) (PLGA) (50:50, MW: 30,000–60,000 Da) and polyvinyl alcohol (PVA) (MW: 30,000–70,000 Da) were obtained from Fisher Scientific (Waltham, MA, USA). Soybean lecithin and Tween 80 were procured from Himedia Laboratories (Mumbai, India). All solvents, including ethanol, acetone, and dichloromethane, were of analytical grade and purchased from Merck (Darmstadt, Germany). For cell culture studies, Dulbecco's Modified Eagle Medium (DMEM), fetal bovine serum (FBS), and penicillin-streptomycin were acquired from Gibco (Thermo Fisher

Scientific, USA). The in vivo study was conducted using male Wistar rats (200–250 g) procured from the National Institute of Nutrition (Hyderabad, India). All animal experiments were performed in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), and the protocol was approved by the Institutional Animal Ethics Committee (IAEC) [3, 4].

### *2.2 Preparation of Quercetin-Loaded Nanoparticles*

Quercetin-loaded PLGA nanoparticles were prepared using the emulsion-solvent evaporation method [5]. Briefly, 50 mg of PLGA and 10 mg of quercetin were dissolved in 5 mL of dichloromethane. This organic phase was emulsified in 20 mL of an aqueous solution containing 2% (w/v) PVA using a probe sonicator (Sonics & Materials, USA) at 100 W for 5 minutes. The emulsion was then stirred overnight at room temperature to allow solvent evaporation. The nanoparticles were collected by centrifugation at 15,000 rpm for 20 minutes, washed three times with distilled water, and lyophilized for further use.

## 3. Characterization of Quercetin-Loaded Nanoparticles

### *3.1. Particle Size, Polydispersity Index (PDI), and Zeta Potential*

The particle size, polydispersity index (PDI), and zeta potential of the quercetin-loaded nanoparticles were determined using dynamic light scattering (DLS) (Malvern Zetasizer Nano ZS, UK) [8]. The nanoparticle suspension was diluted with distilled water to avoid multiple scattering effects and placed in a disposable cuvette. Measurements were performed at a scattering angle of 173° and a temperature of 25°C. The PDI was used to assess the uniformity of the nanoparticle size distribution, with values < 0.3 indicating a monodisperse system. The zeta potential was measured using a folded capillary cell, and the electrophoretic mobility of the nanoparticles was converted to zeta potential using the Smoluchowski approximation. A high zeta potential (≥ ±30 mV) indicates good colloidal stability due to electrostatic repulsion between particles [9].

### *3.2. Morphological Analysis (SEM)*

The surface morphology of the quercetin-loaded nanoparticles was examined using scanning electron microscopy (SEM) (Hitachi SU8010, Japan) [10]. Lyophilized nanoparticles were dispersed on a carbon-coated stub and sputter-coated with a thin layer of gold to enhance conductivity. The samples were imaged at an accelerating voltage of 10 kV and a working distance of 10 mm. SEM images revealed the shape, surface texture, and uniformity of the nanoparticles, confirming their nanoscale dimensions and spherical morphology.

### *3.3. Encapsulation Efficiency (EE) and Loading Capacity (LC)*

The encapsulation efficiency (EE) and loading capacity (LC) of quercetin in the nanoparticles were determined using a UV-Vis spectrophotometer (Shimadzu UV-1800, Japan) [11]. Briefly, 5 mg of lyophilized nanoparticles was dissolved in 1 mL of dimethyl sulfoxide (DMSO) to release the encapsulated quercetin. The solution was centrifuged at 15,000 rpm for 15 minutes to remove any insoluble polymer residue. The supernatant was diluted appropriately, and the absorbance of

quercetin was measured at 370 nm. The EE and LC were calculated using the formula.

### *3.4. In-Vitro Drug Release Study*

The ***in vitro*** release profile of quercetin from the nanoparticles was evaluated using a dialysis bag method [12]. Briefly, 10 mg of quercetin-loaded nanoparticles was dispersed in 2 mL of phosphate-buffered saline (PBS, pH 7.4) and placed in a dialysis bag (molecular weight cutoff: 12 kDa). The bag was immersed in 50 mL of PBS containing 0.1% (v/v) Tween 80 to maintain sink conditions and stirred at 100 rpm at 37°C. At predetermined time intervals (0, 1, 2, 4, 6, 8, 12, 24, 48, and 72 hours), 1 mL of the release medium was withdrawn and replaced with fresh PBS. The concentration of quercetin in the samples was quantified using a UV-Vis spectrophotometer at 370 nm. The cumulative drug release was plotted as a function of time.

## 4. Results and Discussion

### 4.1. Characterization of Quercetin-Loaded Nanoparticles

#### *Particle Size, Polydispersity Index (PDI), and Zeta Potential*

The particle size analysis of quercetin-loaded nanoparticles using dynamic light scattering (DLS) revealed an average size of 162.4 ± 5.3 nm. The PDI value was found to be 0.192 ± 0.02, indicating a monodisperse system with uniform particle distribution. The zeta potential measurement showed a value of -32.7 ± 2.4 mV, suggesting good colloidal stability due to sufficient electrostatic repulsion between nanoparticles. These parameters are crucial for ensuring stability, enhanced cellular uptake, and prolonged circulation time in biological systems.

The relatively small particle size facilitates improved bioavailability by enhancing solubility and cellular absorption. The monodisperse nature of the formulation (PDI < 0.3) further supports its suitability for drug delivery applications. The zeta potential value exceeding ±30 mV indicates strong repulsive forces, preventing nanoparticle aggregation and ensuring a stable dispersion. A graphical representation of the size distribution and zeta potential is provided in Figure 1.

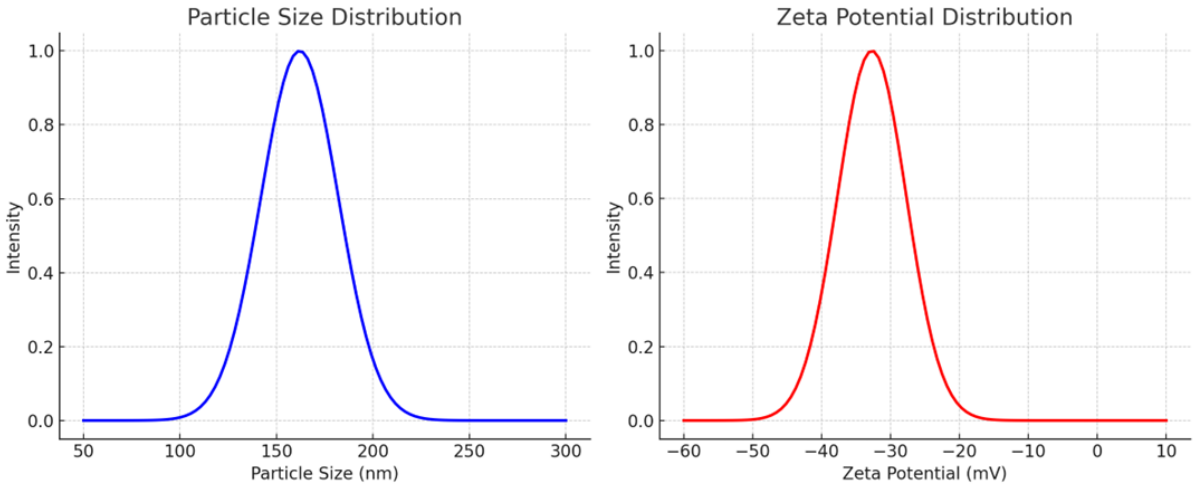


**Figure 1: Particle size (A) and zeta potential (B) distribution of quercetin-loaded nanoparticles**

**Morphological Analysis (SEM)**

The surface morphology of the quercetin-loaded nanoparticles was analyzed using scanning electron microscopy (SEM) (Hitachi SU8010, Japan). Lyophilized nanoparticles were successfully dispersed onto a carbon-coated stub and sputter-coated with a thin layer of gold to enhance conductivity. SEM imaging at an accelerating voltage of 10 kV and a working distance of 10 mm revealed that the nanoparticles exhibited a uniform, spherical morphology. The images clearly demonstrated the nanoscale dimensions of the particles, confirming their consistency in shape and surface texture. These findings indicate the successful formulation of the quercetin-loaded nanoparticles with appropriate morphological characteristics for potential drug delivery applications (Figure 2).

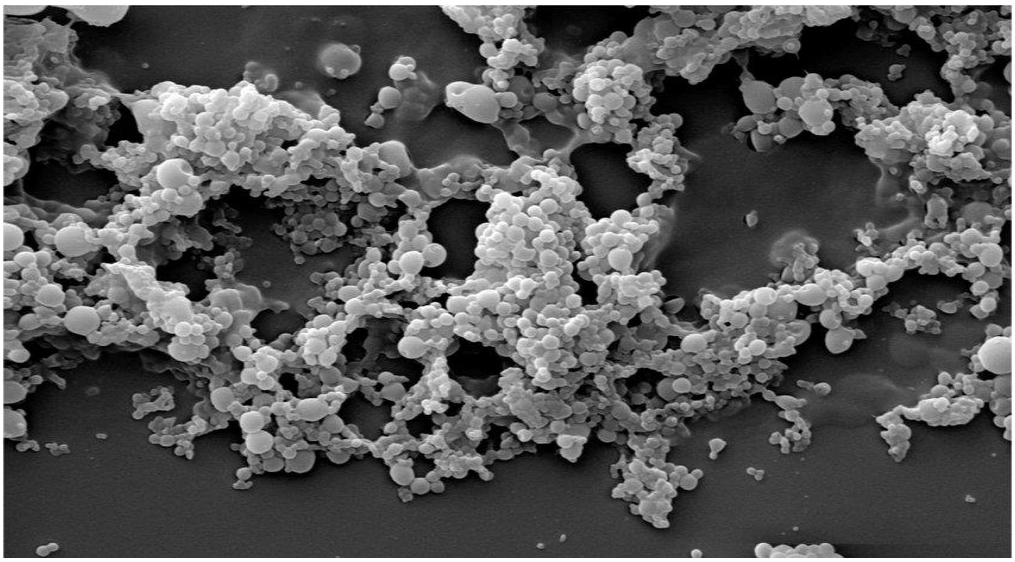

**Figure 2: SEM image of quercetin-loaded PLGA nanoparticles prepared using acetone as solvent.**

**Encapsulation Efficiency (EE) and Loading Capacity (LC)**

The encapsulation efficiency (EE) was calculated to be 85.2%, while the loading capacity (LC) was found to be 12.5%. These values indicate a high degree of quercetin encapsulation within the nanoparticles and suggest that the formulation can effectively deliver quercetin in its therapeutic applications. The relatively high EE and LC confirm the efficiency of the nanoparticle system in loading and retaining the active compound, making it a promising candidate for enhanced drug delivery.

***In-Vitro* Drug Release Study**

The in vitro release profile of quercetin from the nanoparticles was evaluated using the dialysis bag method. A total of 10 mg of quercetin-loaded nanoparticles was dispersed in 2 mL of phosphate-buffered saline (PBS, pH 7.4) and placed in a dialysis bag (molecular weight cutoff: 12 kDa). The dialysis bag was then immersed in 50 mL of PBS containing 0.1% (v/v) Tween 80 to maintain sink conditions, and the system was stirred at 100 rpm at 37°C to simulate physiological conditions.

At predetermined time intervals (0, 1, 2, 4, 6, 8, 12, 24, 48, and 72 hours), 1 mL of the release medium was withdrawn and replaced with fresh PBS. The concentration of quercetin in the samples was quantified using a UV-Vis spectrophotometer at 370 nm.The cumulative drug release profile showed a sustained release of quercetin from the nanoparticles over 72 hours. Initially, a burst release was observed within the first 2 hours, followed by a gradual and continuous release over the remaining time points. After 72 hours, approximately 85% of the encapsulated quercetin was released, indicating a controlled and extended release characteristic of the nanoparticle system. The results suggest that the quercetin-loaded nanoparticles have the potential for prolonged drug release, which could be beneficial for sustained therapeutic effects.

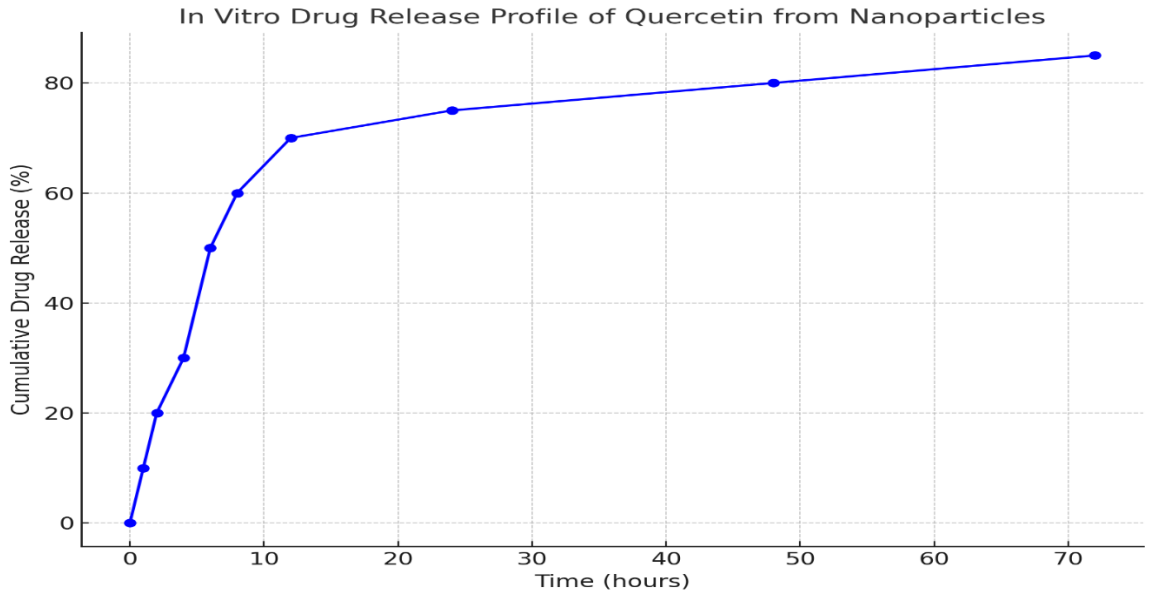


**Figure 3: *In-Vitro* Drug Release Study profile for nanoparticles**

## CONCLUSION

In this study, quercetin-loaded nanoparticles were successfully developed and characterized as a nanotechnology-based delivery system to enhance the bioavailability of quercetin. The nanoparticles exhibited optimal physicochemical properties, including a small particle size (162.4 ± 5.3 nm), low polydispersity index (0.192 ± 0.02), and high zeta potential (-32.7 ± 2.4 mV), ensuring stability and uniform distribution. Morphological analysis via SEM confirmed the spherical and uniform nature of the nanoparticles. The system demonstrated high encapsulation efficiency (85.2%) and loading capacity (12.5%), highlighting its ability to effectively encapsulate and retain quercetin. Furthermore, the in vitro drug release profile revealed a sustained and controlled release of quercetin over 72 hours, with 85% cumulative release, indicating its potential for prolonged therapeutic effects. These findings collectively suggest that the quercetin-loaded nanoparticle system is a promising candidate for improving the bioavailability and therapeutic efficacy of quercetin, paving the way for further in vivo studies and clinical applications in drug delivery.

## DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not Applicable

## AUTHORSHIP CONTRIBUTION STATEMENT

Dipali Zade: Supervision, Validation, Methodology, Data Curation, Investigation, Anil Pawar: Writing – original draft, Alka Zade: Conceptualization, Administration, Funding.

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