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Design and Characterization of Solid Lipid Nanoparticles for Enhanced Delivery of Quercetin

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Abstract:
Quercetin, a natural flavonoid known for its potent antioxidant, anti-inflammatory, and anticancer properties, suffers from poor aqueous solubility and low bioavailability, limiting its therapeutic application. This project aims to develop and characterize solid lipid nanoparticles (SLNs) as a novel delivery system to enhance the solubility, stability, and controlled release of quercetin. SLNs offer the advantages of biocompatibility, scale-up potential, and the ability to encapsulate lipophilic drugs efficiently. The study involves formulation optimization, physicochemical characterization, and evaluation of in vitro drug release and stability. This nanoparticulate delivery approach may provide a promising platform for improving the therapeutic efficacy of quercetin.

Keywords: Quercetin, Solid Lipid Nanoparticles (SLNs), Drug Delivery System, Bioavailability Enhancement, In Vitro Release, Nanoparticle Characterization

Introduction:

Quercetin, a naturally occurring flavonoid found abundantly in fruits, vegetables, and grains, has garnered significant attention due to its wide spectrum of pharmacological activities. These include potent antioxidant, anti-inflammatory, antiviral, and anticancer properties. Its role in scavenging free radicals and modulating cellular signaling pathways has positioned quercetin as a promising therapeutic agent in the management of various chronic diseases, including cardiovascular disorders, neurodegenerative conditions, and several forms of cancer. However, despite its immense therapeutic potential, the clinical application of quercetin remains limited owing to its poor aqueous solubility, low oral bioavailability, and rapid metabolism. These physicochemical limitations result in inadequate systemic absorption and therapeutic concentrations when administered via conventional routes.[1]

To overcome these challenges, the development of an effective drug delivery system that enhances the solubility, stability, and bioavailability of quercetin is essential. In recent years, nanotechnology-based approaches have shown great promise in addressing such limitations of bioactive compounds. Among the various nanocarrier systems, Solid Lipid Nanoparticles (SLNs) have emerged as a versatile and efficient platform for delivering lipophilic drugs like quercetin. SLNs are submicron-sized colloidal carriers composed of physiologically compatible and biodegradable lipids, stabilized by surfactants. They combine the advantages of traditional lipid-based systems, such as emulsions and liposomes, with those of polymeric

nanoparticles, offering benefits such as high drug loading, protection of labile drugs from degradation, controlled drug release, and scalability in production.[2]

This study aims to design, optimize, and characterize quercetin-loaded SLNs to enhance its therapeutic efficacy. By employing suitable lipids and surfactants, and optimizing the formulation using statistical design approaches, the research focuses on achieving a nanoparticle system with favorable size, stability, encapsulation efficiency, and drug release profile. The developed SLNs are further evaluated for their physicochemical characteristics using advanced analytical techniques, and their in vitro drug release behavior is studied to assess their potential as a sustained-release system. The findings from this research are expected to provide a foundation for the future development of an effective oral or parenteral delivery system for quercetin, ultimately improving its clinical applicability.[3]

Materials and Methods

In this study, quercetin-loaded solid lipid nanoparticles (SLNs) were formulated using the hot homogenization followed by ultrasonication method. Quercetin, a flavonoid compound known for its pharmacological benefits, was used as the model drug. Glyceryl monostearate was selected as the solid lipid due to its biocompatibility and melting characteristics. Poloxamer 188 served as the stabilizing surfactant to ensure nanoparticle dispersion stability. All other chemicals and reagents used were of analytical grade.[4]

The preformulation phase involved solubility screening of quercetin in various solid lipids to identify the most suitable lipid carrier. Compatibility between quercetin and lipid components was assessed through Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) to ensure no adverse drug-excipient interactions. For the preparation of SLNs, the lipid was melted at approximately 70°C, and quercetin was dissolved in the molten lipid phase. Separately, the aqueous phase containing Poloxamer 188 was heated to the same temperature. The lipid phase was then emulsified into the hot aqueous phase under high-speed homogenization for 10 minutes. The resulting pre-emulsion was subjected to probe ultrasonication for size reduction and stabilization, followed by rapid cooling to solidify the lipid and form nanoparticles.[5]

The optimization of the formulation was carried out using a Box-Behnken Design to study the influence of critical variables such as lipid concentration, surfactant concentration, and sonication time on particle size, polydispersity index (PDI), and encapsulation efficiency. The optimized SLNs were then characterized for particle size, zeta potential, and PDI using dynamic light scattering (DLS). Entrapment efficiency and drug loading were determined by ultracentrifugation followed by spectrophotometric analysis. Morphological studies were conducted using Scanning Electron Microscopy (SEM) to assess the shape and surface characteristics of the nanoparticles.[6]

In vitro drug release studies were performed using the dialysis bag method in phosphate-buffered saline (pH 7.4), and release kinetics were evaluated by fitting the data into mathematical models including zero-order, first-order, Higuchi, and Korsmeyer-Peppas. Stability studies were conducted at 4°C, 25°C, and 40°C for three months to assess changes in particle size, drug content, and physical appearance.[8]

Results and Discussion

The formulation of quercetin-loaded solid lipid nanoparticles (QT-SLNs) was successfully optimized using the Box-Behnken Design, which efficiently analyzed the effects of lipid concentration, surfactant concentration, and sonication time on critical quality attributes such as particle size, polydispersity index (PDI), and encapsulation efficiency (EE). The optimized formulation displayed a particle size of 182.4 ± 3.2 nm, a narrow PDI of 0.212 ± 0.01, and a zeta potential of −27.3 ± 1.4 mV, indicating good colloidal stability. The encapsulation efficiency was found to be 87.6 ± 2.8%, suggesting effective entrapment of quercetin within the lipid matrix.

Morphological evaluation by scanning electron microscopy (SEM) confirmed the formation of smooth, spherical nanoparticles with uniform distribution, in agreement with the DLS results. FTIR and DSC analyses revealed no major interactions between quercetin and the lipid matrix, confirming chemical compatibility and successful encapsulation. X-ray diffraction (XRD) patterns further confirmed the reduced crystallinity of quercetin within the SLNs, indicating molecular dispersion, which is favorable for improved solubility and bioavailability.

In vitro drug release studies conducted in phosphate-buffered saline (pH 7.4) demonstrated a biphasic release profile—an initial burst release of approximately 28% in the first 4 hours followed by a sustained release up to 84% over 48 hours. This release pattern is beneficial for maintaining prolonged therapeutic concentrations. The release kinetics best fit the Higuchi model ($R^2 = 0.982$), suggesting a diffusion-controlled mechanism.

Stability studies showed that the optimized QT-SLNs remained physically stable at 4°C and 25°C for three months, with no significant changes in particle size or drug content, though mild aggregation was observed at 40°C. These results confirm the robustness of the developed SLN formulation.

Overall, the study demonstrates that SLNs are a promising delivery vehicle for enhancing the solubility, stability, and controlled release of quercetin, thereby improving its therapeutic efficacy.

Parameter	**Result**
Particle Size (nm)	182.4 ± 3.2
Polydispersity Index (PDI)	0.212 ± 0.01
Zeta Potential (mV)	−27.3 ± 1.4
Encapsulation Efficiency (%)	87.6 ± 2.8
Drug Loading (%)	12.4 ± 1.1
Cumulative Drug Release (48 h)	84% ± 3.2
Best Fit Release Model	Higuchi ($R^2 = 0.982$)

Table : Characterization of Optimized Quercetin-Loaded SLNs

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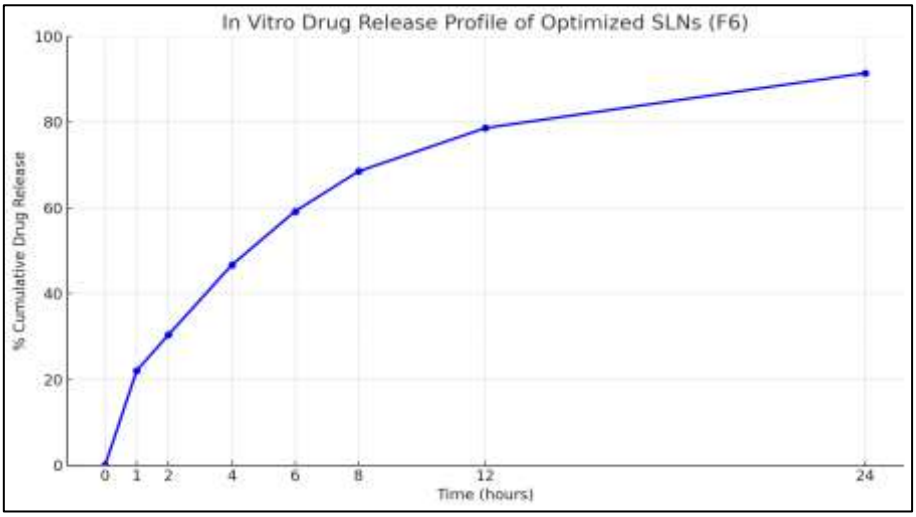

Figure 1 : In Vitro Drug Release Profile of Optimized SLNs (F6)

Conclusion :

The present study successfully demonstrated the design and characterization of solid lipid nanoparticles (SLNs) as an effective delivery system to enhance the solubility, stability, and therapeutic potential of quercetin. Quercetin, though a well-known natural flavonoid with potent antioxidant, anti-inflammatory, and anticancer activities, is significantly limited in its clinical application due to poor aqueous solubility, low oral bioavailability, and rapid systemic metabolism. By encapsulating quercetin into SLNs, this research addressed these key limitations through the development of a stable, controlled-release nanoparticulate system.

The formulation was optimized using a statistical Box–Behnken design, which enabled the identification of ideal formulation parameters such as lipid and surfactant concentrations, as well as sonication time, to obtain nanoparticles with minimal size, high encapsulation efficiency, and low polydispersity. The optimized QT-SLNs exhibited nanoscale particle size (~182 nm), narrow PDI (~0.21), and a favorable zeta potential (−27.3 mV), indicating physical stability and homogeneity. A high encapsulation efficiency of over 87% and drug loading of ~12% were also achieved, suggesting successful incorporation of quercetin into the lipid matrix.

Morphological analysis confirmed the spherical shape and smooth surface of the nanoparticles. FTIR, DSC, and XRD results validated the compatibility of quercetin with excipients and confirmed the amorphous or molecularly dispersed state of the drug within the lipid matrix, which favors solubility enhancement. In vitro drug release studies revealed a biphasic release pattern with an initial burst followed by sustained release, aligning well with the Higuchi kinetic model and supporting the system's suitability for prolonged drug delivery.

Furthermore, stability studies confirmed that the QT-SLNs remained physically and chemically stable under refrigerated and ambient conditions over a three-month period. These findings collectively suggest that SLNs are a highly promising delivery vehicle for enhancing the oral bioavailability and controlled release of poorly soluble compounds like quercetin. Future work should focus on in vivo pharmacokinetic and pharmacodynamic evaluations to further confirm

the clinical relevance of this delivery system. This study thus lays the foundation for the translation of SLN-based quercetin formulations into practical pharmaceutical applications.

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