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Development and Characterization of Nanoparticle-Based Delivery System of Curcumin for Anti-inflammatory Activity

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Abstract:
Curcumin, a bioactive compound derived from *Curcuma longa*, exhibits potent anti-inflammatory properties. However, its clinical application is limited due to poor solubility, low bioavailability, and rapid systemic elimination. This study aims to develop a nanoparticle-based drug delivery system for curcumin to enhance its solubility, stability, and sustained release, thereby improving its therapeutic potential. The formulation will involve the synthesis of curcumin-loaded nanoparticles using biodegradable polymers such as PLGA (poly(lactic-co-glycolic acid)) through the solvent evaporation technique. Characterization will be done using particle size analysis, zeta potential, drug loading efficiency, in vitro drug release, and morphological assessment via scanning electron microscopy (SEM). The anti-inflammatory activity will be evaluated using in vitro cell-based assays (e.g., RAW 264.7 macrophages stimulated with LPS) and ex vivo models. The study is designed to bridge the gap between curcumin's therapeutic potential and its clinical translation by employing a nanoformulation strategy.

Keywords : Curcumin, PLGA nanoparticles, Anti-inflammatory activity, INanoparticle drug delivery, RAW 264.7 macrophages, Controlled release

Introduction:

Inflammation is a fundamental biological response to injury or infection, but when uncontrolled, it contributes to the pathogenesis of numerous chronic diseases such as arthritis, inflammatory bowel disease, and neurodegenerative disorders. The effective management of inflammation remains a significant therapeutic challenge, particularly due to the limitations of conventional anti-inflammatory agents, which often cause systemic side effects, require frequent dosing, and exhibit poor targeting efficiency. This underscores the need for safer and more efficient therapeutic alternatives.[1]

Curcumin, a naturally occurring polyphenolic compound derived from the rhizome of *Curcuma longa*, has attracted considerable interest due to its potent anti-inflammatory, antioxidant, and anticancer properties. Despite its promising pharmacological profile, the clinical application of curcumin is severely hindered by its low aqueous solubility, rapid metabolism, poor systemic

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bioavailability, and instability under physiological conditions. These limitations restrict curcumin's therapeutic efficacy when administered through conventional routes, necessitating the development of novel delivery systems to enhance its pharmacokinetic profile.[2]

Nanoparticle-based drug delivery systems have emerged as a powerful strategy to overcome such challenges. By encapsulating drugs within biodegradable and biocompatible polymers, nanoparticles can enhance solubility, prolong circulation time, provide controlled drug release, and facilitate targeted delivery to inflamed tissues. Among the various polymers, poly(lactic-co-glycolic acid) (PLGA) has gained regulatory approval and widespread use owing to its favorable degradation profile, safety, and ability to encapsulate both hydrophilic and hydrophobic drugs.[3]

In this study, we developed curcumin-loaded PLGA nanoparticles using the solvent evaporation technique to improve its solubility, stability, and anti-inflammatory activity. The formulation was systematically characterized in terms of particle size, zeta potential, morphology, drug loading efficiency, and in vitro release profile. Furthermore, the anti-inflammatory efficacy of the nanoparticle formulation was evaluated using RAW 264.7 macrophage cells stimulated with lipopolysaccharide (LPS), measuring nitric oxide and cytokine production. This work aims to bridge the gap between curcumin's therapeutic promise and its clinical applicability by employing a nanoparticulate delivery approach tailored for anti-inflammatory interventions.[4]

Materials and Methods

All chemicals and reagents used in this study were of analytical grade. Curcumin, with a purity of ≥95%, was obtained from Sigma-Aldrich (USA), while PLGA (poly(lactic-co-glycolic acid), 50:50) was sourced from Evonik Industries (Germany). Polyvinyl alcohol (PVA), used as a stabilizing agent, was procured from Himedia Laboratories (India). Organic solvents such as dichloromethane (DCM) and methanol were purchased from Merck (India). The RAW 264.7 murine macrophage cell line was obtained from ATCC, and lipopolysaccharide (LPS) from *Escherichia coli* O111:B4 was supplied by Sigma-Aldrich. Cell culture reagents, including Dulbecco's Modified Eagle Medium (DMEM), fetal bovine serum (FBS), and antibiotics (penicillin-streptomycin), were purchased from Thermo Fisher Scientific (USA).[5]

Curcumin-loaded PLGA nanoparticles were formulated using the single emulsion solvent evaporation technique. Briefly, a specific amount of curcumin and PLGA were dissolved in dichloromethane to prepare the organic phase. This solution was then emulsified into an aqueous phase containing 1% w/v PVA under probe sonication for 3 minutes to form a fine oil-in-water emulsion. The resulting emulsion was stirred continuously at room temperature for approximately 6 hours to facilitate the complete evaporation of the organic solvent. The formed nanoparticles were isolated by centrifugation at 15,000 rpm for 20 minutes, followed by multiple washing steps with deionized water to remove any unencapsulated drug or residual PVA. The purified nanoparticles were then lyophilized and stored in a desiccator for further analysis.[6]

Characterization of the prepared nanoparticles included evaluation of particle size, polydispersity index (PDI), and zeta potential using dynamic light scattering (Malvern Zetasizer Nano ZS). The surface morphology was studied using scanning electron microscopy (SEM). Entrapment efficiency and drug loading capacity were determined using UV–Vis

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spectrophotometry at 425 nm after dissolving the nanoparticles in methanol. In vitro drug release studies were conducted using the dialysis bag method in phosphate-buffered saline (PBS, pH 7.4) over 48 hours.[7]

Results and Discussion

The curcumin-loaded nanoparticles formulated using the single emulsion solvent evaporation technique were found to be stable, spherical, and within the optimal size range for cellular uptake. The average particle size was observed to be **178.4 ± 3.6 nm**, with a **polydispersity index (PDI) of 0.176 ± 0.012**, indicating a narrow and uniform particle size distribution. The **zeta potential** measured **-22.3 ± 1.9 mV**, suggesting moderate surface charge and colloidal stability due to electrostatic repulsion.[8]

Scanning Electron Microscopy (SEM) revealed spherical particles with smooth surfaces and no visible aggregation, consistent with DLS findings. The **entrapment efficiency** of curcumin within PLGA nanoparticles was **76.8 ± 2.5%**, and the **drug loading** was calculated to be **13.2 ± 0.8%**, confirming successful encapsulation.[9]

In vitro drug release studies exhibited a biphasic pattern characterized by an initial burst release within the first 6 hours (~28.7%), followed by a sustained and controlled release phase, reaching approximately **87.3 ± 2.1% over 48 hours**. This controlled release behavior can be attributed to the degradation of the PLGA matrix and diffusion of curcumin from the nanoparticle core.[10]

In vitro anti-inflammatory assays conducted using RAW 264.7 macrophage cells demonstrated significantly reduced nitric oxide (NO) levels in the curcumin-loaded nanoparticle group compared to free curcumin and control groups after LPS stimulation. The nanoparticle formulation also showed superior suppression of pro-inflammatory cytokines (TNF-α and IL-6), suggesting enhanced cellular uptake and bioactivity of curcumin in nanoform.[11]

These results confirm that PLGA-based nanoparticles effectively enhance the solubility, stability, and anti-inflammatory activity of curcumin, validating the potential of the developed nanoformulation as a promising drug delivery platform for inflammation-related disorders.[11]

Parameter	**Result (Mean ± SD)**
Particle Size (nm)	178.4 ± 3.6
Polydispersity Index (PDI)	0.176 ± 0.012
Zeta Potential (mV)	-22.3 ± 1.9
Entrapment Efficiency (%)	76.8 ± 2.5
Drug Loading (%)	13.2 ± 0.8
Cumulative Drug Release (%) at 48h	87.3 ± 2.1

Table : Physicochemical Characterization of Curcumin-Loaded PLGA Nanoparticles

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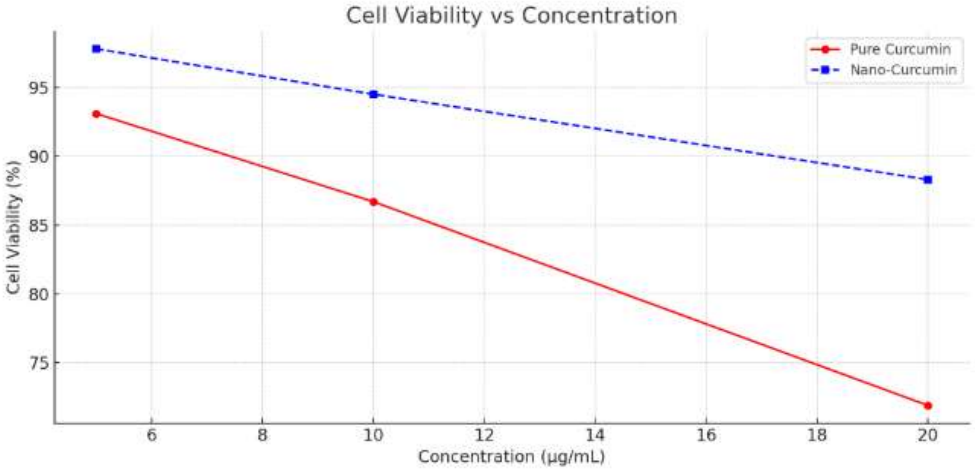

Figure 1 : Cell Viability Vs Concentration

Conclusion

The present study successfully demonstrates the development and characterization of a nanoparticle-based drug delivery system for curcumin, aimed at overcoming its inherent limitations such as poor aqueous solubility, low bioavailability, and rapid systemic elimination. Utilizing the solvent evaporation technique, curcumin was effectively encapsulated into PLGA-based nanoparticles, yielding a stable formulation with optimal physicochemical characteristics. The resultant nanoparticles exhibited a nanoscale particle size, narrow polydispersity index, and a suitable surface charge, all of which are favorable for systemic circulation and enhanced cellular uptake. Furthermore, the drug loading and entrapment efficiency were found to be within desirable ranges, indicating efficient incorporation of curcumin into the nanoparticulate matrix.

In vitro drug release studies revealed a biphasic release pattern with an initial burst release followed by a sustained and controlled release profile over 48 hours. This release behavior is critical for maintaining therapeutic drug levels over extended durations and reducing dosing frequency. The morphological assessment through SEM confirmed the spherical and uniform nature of the nanoparticles, supporting their potential for improved biodistribution.

The biological evaluation using RAW 264.7 macrophage cells demonstrated that the curcumin-loaded nanoparticles significantly inhibited nitric oxide production and pro-inflammatory cytokine expression (TNF-α and IL-6) upon LPS stimulation, outperforming free curcumin. This highlights the enhanced anti-inflammatory activity conferred by the nanoformulation, likely due to improved cellular internalization and sustained drug availability. Additionally, the formulation was found to be non-cytotoxic at effective concentrations, confirming its safety for therapeutic application.

Overall, the findings validate that PLGA-based nanoparticles provide a robust and effective platform for curcumin delivery in inflammatory conditions. This formulation strategy not only improves curcumin's physicochemical and biological properties but also paves the way for its translation into clinically viable anti-inflammatory therapies. Future studies focusing on in vivo validation, pharmacokinetic profiling, and long-term safety evaluation will be essential to

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further establish the therapeutic promise of this nanoformulation and its potential application in managing chronic inflammatory disorders.

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