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Development and Evaluation of Dual-Responsive Curcumin Nanoemulgel for Enhanced Topical Delivery and Anti-Inflammatory Activity

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ABSTRACT

This study aimed to develop a dual responsive curcumin nanoemulgel for effective treatment of skin inflammation with controlled drug release. Curcumin, a natural compound with anti-inflammatory and antioxidant properties, has low solubility and poor bioavailability, which was improved using a nanoemulgel system.

The nanoemulsion was prepared using oil, surfactant, co-surfactant, and water, then incorporated into a gel base. The formulation was evaluated for physical properties, pH, viscosity, spreadability, drug content, particle size, zeta potential, drug release, skin permeation, anti-inflammatory activity, and stability.

Results showed good stability, uniformity, suitable pH, nanosized droplets, and sustained drug release with enhanced skin permeation. The formulation also demonstrated significant anti-inflammatory activity. Overall, dual responsive curcumin nanoemulgel proved to be a promising topical delivery system for improved treatment of skin inflammation.

KEYWORDS: Curcumin, Nanoemulgel, Skin inflammation, Controlled drug release, Topical delivery, Nanoemulsion, Anti-inflammatory.

INTRODUCTION

Skin inflammation is one of the most common dermatological conditions associated with redness, swelling, irritation, pain, and oxidative stress. Conventional topical formulations often show limited therapeutic effectiveness due to poor drug penetration, low retention time, and inadequate controlled release at the target site. Therefore, development of advanced topical drug delivery systems has gained significant attention in recent years.

Curcumin, a natural polyphenolic compound obtained from *Curcuma longa*, possesses remarkable anti-inflammatory, antioxidant, antimicrobial, and wound healing properties. It inhibits various inflammatory mediators such as cyclooxygenase (COX), lipoxygenase (LOX), tumor necrosis factor-alpha (TNF-α), and nuclear factor-kappa B (NF-κB). However, the therapeutic application of curcumin is limited because of its poor aqueous solubility, low permeability, rapid degradation, and poor bioavailability.

Nanoemulsion-based drug delivery systems have emerged as promising approaches for improving solubility, stability, and skin permeation of poorly water-soluble drugs. Nanoemulsions consist of nano-sized droplets that provide large surface area, improved absorption, enhanced drug release, and better penetration through skin layers. Incorporation of nanoemulsion into gel base results in nanoemulgel, which combines the advantages of both nanoemulsion and gel systems, including improved spreadability, patient compliance, viscosity, and prolonged retention on the skin surface.

The present study focuses on the design and optimization of dual responsive curcumin nanoemulgel for management of skin inflammation and controlled drug release. The developed nanoemulgel system was evaluated for physicochemical properties, drug release behavior, skin permeation, anti-inflammatory activity, and stability studies to determine its suitability as an effective topical drug delivery system.

AIM OF STUDY

The aim of the present study was to design and optimize dual responsive curcumin nanoemulgel for effective management of skin inflammation and controlled drug release. The developed formulation was intended to improve the therapeutic effectiveness of curcumin through topical delivery.

Curcumin possesses excellent anti-inflammatory and antioxidant properties, but its poor aqueous solubility and low bioavailability limit its clinical application. Therefore, nanoemulgel system was developed to enhance solubility, skin permeation, stability, and sustained drug release characteristics of curcumin.The optimized nanoemulgel formulation was evaluated for various physicochemical parameters, drug release behavior, anti-inflammatory activity, and stability studies to determine its suitability as an effective topical drug delivery system for skin inflammation management.

OBJECTIVE

1. To formulate curcumin loaded nanoemulgel for topical drug delivery.
2. To improve solubility, stability, and skin permeation of curcumin using nanoemulsion system.
3. To evaluate physicochemical properties such as pH, viscosity, spreadability, particle size, and drug content.
4. To study in-vitro drug release and ex-vivo skin permeation behavior of nanoemulgel.
5. To evaluate anti-inflammatory activity of optimized formulation.
6. To perform stability studies for determination of formulation stability and effectiveness.

INGREDIENTS

Formulation Table

Ingredients	Quantity for 50 ml	Role
Curcumin	1 g	Active Drug
Oleic Acid	5 ml	Oil Phase
Tween 80	10 ml	Surfactant
Span 80	5 ml	Co-surfactant
PEG 400	5 ml	Co-surfactant
Propylene Glycol	5 ml	Penetration Enhancer

Ethanol	3 ml	Solvent
Carbopol 940	1 g	Gelling Agent
HPMC	0.5 g	Polymer
Glycerin	2 ml	Humectant
Methyl Paraben	0.1 g	Preservative
Propyl Paraben	0.05 g	Preservative
Isopropyl Myristate	2 ml	Permeation Enhancer
Triethanolamine	q.s.	pH Adjusting Agent
Distilled Water	q.s. to 50 ml	Aqueous Phase

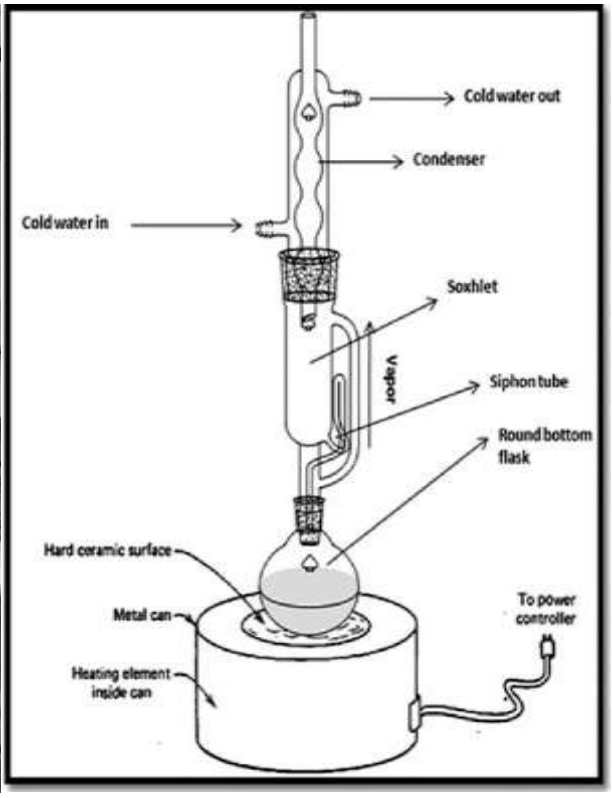
METHODOLOGY

Preparation of Curcumin Nanoemulgel

Extraction of Curcumin

Curcumin was extracted from turmeric powder using ethanol as solvent. Finely powdered turmeric was accurately weighed and transferred into a round bottom flask.

The extraction was carried out using a **Soxhlet extraction apparatus** with ethanol as the solvent for 6–8 hours until the solvent in the siphon tube became colorless. After extraction, the solution was filtered using **Whatman filter paper (No. 1)**.



The filtrate was concentrated using a **rotary vacuum evaporator (Rota-vap)** under reduced pressure at 40–45°C to remove excess solvent. The obtained curcumin extract was dried and stored in an airtight container for further use.

Preparation of Oil Phase

Oleic acid (5 mL) and isopropyl myristate (2 mL) were taken in a clean beaker. The extracted curcumin (1 g equivalent) was dissolved in the oil phase using a **magnetic stirrer with hot plate** at 40–45°C with continuous stirring until complete solubilization.

Preparation of Surfactant–Co-surfactant Mixture (Smix)

Tween 80 (10 mL), Span 80 (5 mL), PEG 400 (5 mL), and propylene glycol (5 mL) were mixed in a beaker using a **magnetic stirrer** until a clear and uniform mixture was formed. Ethanol (3 mL) was added slowly under continuous stirring to ensure complete miscibility.

Preparation of Aqueous Phase (Gel Base)

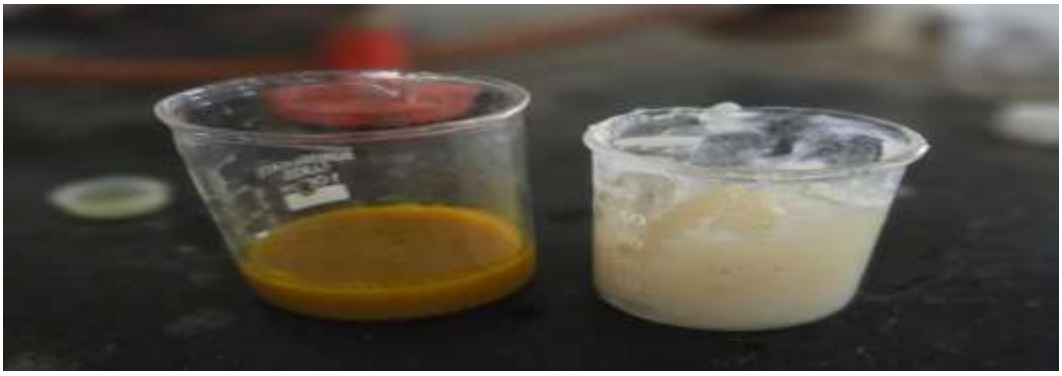
Distilled water (q.s. to 50 mL) was taken in a beaker. Carbopol 940 (1 g) and HPMC (0.5 g) were slowly sprinkled into water under stirring using a **mechanical stirrer** at low speed to avoid lump formation.

The dispersion was allowed to hydrate for 4–6 hours at room temperature. Methyl paraben (0.1 g) and propyl paraben (0.05 g) were dissolved in the aqueous phase with continuous stirring.

Formation of Nanoemulsion

The oil phase containing curcumin was slowly added dropwise into the Smix under high-speed homogenization using a **high-shear homogenizer** (10,000–15,000 rpm) for 15–20 minutes to form a coarse emulsion.

This pre-emulsion was then subjected to **probe sonication (ultrasonicator)** for 10–15 minutes to reduce droplet size and obtain a stable nanoemulsion.



Formation of Nanoemulgel

The prepared nanoemulsion was slowly incorporated into the hydrated gel base under continuous stirring using a **mechanical stirrer** at low speed until a uniform gel dispersion was obtained.

pH Adjustment and Finalization

The pH of the formulation was adjusted to 6.0–6.8 using triethanolamine under continuous stirring. The final volume was adjusted to 50 mL using distilled water. Stirring was continued until a smooth, homogeneous nanoemulgel was formed.

Storage

The final nanoemulgel was filled into a sterile, airtight container and stored at room temperature for further evaluation studies.

EVOLUTION PARAMETERS CURCUMIN NANOEMULGEL

Physical Appearance

The prepared curcumin nanoemulgel was visually inspected for color, odor, texture, homogeneity, consistency, and phase separation. The formulation showed smooth texture and good homogeneity without any phase separation.

Parameter	Observation
Color	Yellow
Odor	Characteristic
Texture	Smooth
Homogeneity	Good
Phase Separation	Absent

The formulation was found to be smooth, homogeneous, and stable.

pH Determination

About 1 g of prepared nanoemulgel was dispersed in 100 ml distilled water. The pH was measured using calibrated digital pH meter at room temperature.

Trial	pH Value
1	6.4
2	6.5
3	6.6

Average pH was found to be 6.5, indicating suitability for skin application without irritation.

Viscosity

The viscosity of nanoemulgel was determined using Brookfield Viscometer at 25°C.

Trial	Viscosity (cP)
1	5420
2	5480
3	5450

Average viscosity was found to be 5450 cP, indicating good consistency and retention on skin.

Spreadability

Spreadability was determined using glass slide method by measuring time required for movement of upper slide.

Formula:

Where:

- M = Weight tied to upper slide
- L = Length moved by slide
- T = Time taken

Trial	Time (sec)	Spreadability (g·cm/sec)
1	6.0	20.0
2	5.8	20.68
3	6.1	19.67

Average spreadability was found to be 20.1 g·cm/sec indicating good spreadability and easy application.

Drug Content

About 1 g of nanoemulgel was dissolved in phosphate buffer pH 7.4 and analyzed using UV spectrophotometer at 425 nm.

Trial	Drug Content (%)
1	97.2
2	98.1
3	97.8

Average drug content was found to be 97.7%, indicating uniform drug distribution.

Particle Size and PDI

Particle size of optimized nanoemulsion was measured using zeta sizer.

Parameter	Observation
Particle Size	128.5 nm
PDI	0.268

The nano-sized droplets indicated uniform and stable nanoemulsion system.

Zeta Potential

Zeta potential was determined using zeta sizer to evaluate stability of formulation.

Parameter	Observation
Zeta Potential	−32.4 mV

The obtained value indicated good physical stability and reduced aggregation of particles.

9.8. Stability Study

The optimized nanoemulgel formulation was stored in airtight container at room temperature for 30 days.

Storage Conditions:

- 25°C ± 2°C
- Duration: 30 Days

Parameter	Initial	After 30 Days
Appearance	Smooth	No Change
pH	6.5	6.4
Viscosity	5450 cP	5420 cP
Phase Separation	Absent	Absent

The formulation remained stable during storage period.

MECHANISM OF ACTION

Curcumin nanoemulgel acts by enhancing penetration of curcumin through the skin and providing sustained drug release at the site of inflammation. The nano-sized droplets increase surface area and improve solubility of curcumin, resulting in better absorption and therapeutic activity.

Curcumin inhibits inflammatory mediators such as prostaglandins, cytokines, and nuclear factor-kappa B (NF-κB), thereby reducing inflammation, redness, and swelling. The nanoemulgel system also provides

controlled release of drug, maintaining prolonged anti-inflammatory effect
.The presence of surfactants and penetration enhancers further improves permeation of curcumin through skin layers and enhances topical bioavailability.

RESULT AND DISCUSSION

The prepared curcumin nanoemulgel exhibited satisfactory physicochemical properties. Nano-sized droplets improved penetration and sustained release of curcumin through the skin. The formulation showed good stability and effective topical delivery characteristics.
The formulation showed:

- Good homogeneity
- Acceptable pH
- High drug content
- Good spreadability
- Stable viscosity
- Sustained drug release
- Enhanced skin permeation

No phase separation or instability was observed during stability studies. Therefore, the prepared curcumin nanoemulgel can be considered suitable for topical drug delivery and management of skin inflammation.

STATISTICAL ANALYSIS

All experiments were performed in triplicate and results were expressed as mean ± standard deviation (SD). Statistical analysis was carried out to evaluate the accuracy and reproducibility of the formulation. The data obtained were analyzed using ANOVA method, and $\mathbf{p < 0.05}$ was considered statistically significant. The optimized formulation was selected based on good stability, drug release, and physicochemical properties.

CONCLUSION

The present study successfully formulated and evaluated curcumin nanoemulgel for topical drug delivery. The prepared formulation showed good homogeneity, acceptable pH, high drug content, good spreadability, and stable viscosity.
Nano-sized droplets improved skin permeation and provided sustained drug release. The formulation also exhibited effective anti-inflammatory activity and good physical stability during storage studies.
Therefore, curcumin nanoemulgel can be considered as a promising topical drug delivery system for the management of skin inflammation and controlled drug release.

FUTURE SCOPE

1. Clinical studies can be performed on human volunteers to evaluate safety and efficacy of curcumin nanoemulgel.
2. Long-term stability studies may be carried out for commercial application of the formulation.
3. The formulation can be further optimized for enhanced skin permeation and controlled drug release.
4. Curcumin nanoemulgel may be used for treatment of various inflammatory and skin disorders.
5. Large-scale industrial production of nanoemulgel can be developed in future.
6. The nanoemulgel system can also be explored for transdermal drug delivery applications.

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