INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Paper

Curcumin And Tea Tree Oil-Loaded Niosomal Gel with Aloe Vera: A Polyherbal Approach to Anti-Acne Therapy

Swetha V*, Navyashree V, Chandana V, Amaldev K M, Abin T S, Anju K P

Department of Pharmaceutics, Spurthy College of Pharmacy, Rajiv Gandhi University of Health Sciences, Bengaluru, India – 560002.

ARTICLE INFO

Published: 21 Sept 2026
Keywords:
Curcumin; Tea Tree Oil; Niosomes; Niosomal Gel; Aloe vera; Acne.
DOI:
10.5281/zenodo.22867615

ABSTRACT

Acne vulgaris is a prevalent inflammatory skin condition that commonly affects adolescents and young adults. The limitations associated with conventional topical preparations have encouraged the exploration of natural bioactive compounds and advanced drug delivery systems for topical application. The present study focused on the development of a polyherbal niosomal gel containing Curcumin and Tea Tree Oil enriched with Aloe vera as a potential topical approach for acne management. Preformulation investigations were performed for Curcumin and Tea Tree Oil to establish their physicochemical characteristics and suitability for formulation development. Niosomal formulations were prepared and subjected to evaluation for appearance, homogeneity, pH, particle size, zeta potential, entrapment efficiency, and drug content. Based on the obtained evaluation parameters, F3 was selected as the optimized niosomal formulation. The optimized niosomal dispersion was subsequently incorporated into a Carbopol 934 gel base enriched with Aloe vera. The resulting gel formulations were assessed for appearance, homogeneity, pH, viscosity, spreadability, extrudability, and drug content. Among the prepared formulations, G3 was identified as the optimized niosomal gel. F3 exhibited a particle size of 286.0 nm with a PDI of 0.287, while G3 demonstrated suitable physicochemical characteristics for topical application. Overall, the study indicates that the developed Curcumin and Tea Tree Oil-loaded niosomal gel enriched with Aloe vera has potential as a polyherbal topical formulation for the management of acne.

INTRODUCTION

1.1 Acne Vulgaris

Acne vulgaris is a common chronic inflammatory disorder of the pilosebaceous unit that

***Corresponding Author:** Swetha V
Address: *Department of Pharmaceutics, Spurthy College of Pharmacy, Rajiv Gandhi University of Health Sciences, Bengaluru, India – 560002.*
Email ✉: velswetha4@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

predominantly affects adolescents and young adults. It is mainly observed on the face, chest, shoulders, and back, where sebaceous glands are abundant. The development of acne is associated with multiple factors that act together during disease progression.[1]

The major factors involved in acne development include:

- Increased sebum production
- Abnormal follicular keratinization
- Proliferation of Cutibacterium acnes
- Release of inflammatory mediators
- Obstruction of the pilosebaceous follicles [1]

Depending on its severity, acne may present as comedones, papules, pustules, nodules, or cystic lesions. Persistent or severe acne may result in post-inflammatory pigmentation, permanent scarring, and psychological distress.[2]

1.2 Limitations of Conventional Acne Therapy

Topical therapy is an important approach for acne management because the formulation can be applied directly to the affected skin. Common topical agents include retinoids, benzoyl peroxide, antibiotics, salicylic acid, and azelaic acid.[3]

Despite their therapeutic usefulness, conventional topical treatments may have certain limitations:[3]

- Skin dryness and irritation
- Burning sensation and erythema
- Photosensitivity with certain agents
- Poor tolerability during prolonged treatment
- Development of antimicrobial resistance with repeated antibiotic use [4]

These limitations have encouraged the investigation of naturally derived bioactive compounds and advanced topical delivery systems for acne management.[4]

1.3 Curcumin

Curcumin is a naturally occurring polyphenolic compound obtained from ***Curcuma longa***. It possesses several biological activities, including anti-inflammatory, antioxidant, and antimicrobial properties, which make it a promising candidate for dermatological applications.[5]

The potential relevance of curcumin in acne management is associated with:

- Anti-inflammatory activity that may help address inflammatory processes
- Antioxidant activity that may provide protection against oxidative stress
- Antimicrobial activity that may support management of microbial involvement in acne 5

However, the topical application of curcumin is challenged by its poor aqueous solubility and limited delivery through conventional formulations. Therefore, an appropriate drug delivery system may be beneficial for improving its incorporation and topical application.[6]

1.4 Tea Tree Oil

Tea Tree Oil is a natural essential oil obtained from ***Melaleuca alternifolia*** and is widely investigated for its dermatological applications. It possesses antimicrobial and anti-inflammatory properties that make it a promising natural ingredient for topical acne preparations.[7]

Its potential usefulness in acne therapy can be attributed to:

- Antimicrobial activity against microorganisms associated with acne
- Anti-inflammatory activity that may support management of inflammatory lesions
- Natural origin and suitability for incorporation into topical preparations [7]

However, the development of a suitable formulation is important to ensure uniform distribution, convenient application, and acceptable physicochemical properties of Tea Tree Oil. [8]

1.5 Aloe Vera

Aloe vera is a commonly used botanical ingredient in topical and dermatological preparations. It is associated with soothing, moisturizing, skin-conditioning, and anti-inflammatory properties. [9]
In the present formulation, Aloe vera serves as a supportive botanical component of the gel base. Its incorporation may contribute to:

- Improved skin feel and soothing effect
- Moisturizing properties
- Supportive activity for irritated or inflamed skin
- Better suitability of the formulation for topical application

Thus, Aloe vera provides an additional botanical component to the proposed polyherbal topical system.[9]

1.6 Niosomal Drug Delivery System

Niosomes are vesicular drug delivery systems formed primarily using non-ionic surfactants along with suitable stabilizing components. Their vesicular structure provides an opportunity to incorporate different types of active pharmaceutical ingredients and natural bioactive compounds.[10]
Niosomes are considered useful for topical delivery because they may:

- Improve incorporation of poorly soluble active compounds
- Provide protection to incorporated bioactive substances
- Enhance interaction of the formulation with the skin
- Promote localized delivery of active ingredients
- Provide potential control over drug release 11

These characteristics make niosomes a promising carrier system for the topical delivery of natural compounds such as curcumin and Tea Tree Oil.

1.7 Niosomal Gel

Although niosomes can provide advantages as a vesicular delivery system, incorporation of the optimized niosomal dispersion into a gel base can improve its practical application as a topical dosage form.[12]
A niosomal gel can provide:

- Easy application to the skin
- Good spreadability
- Suitable viscosity for topical use
- Prolonged contact with the application site
- Convenient administration compared with a liquid dispersion [12]

In the present study, the optimized Curcumin and Tea Tree Oil-loaded niosomal dispersion was incorporated into a Carbopol 934 gel base enriched with Aloe vera to obtain a suitable topical formulation.

1.8 Rationale of the Study

Curcumin, Tea Tree Oil, and Aloe vera possess different but complementary properties that may be beneficial for topical acne management. However, the formulation of natural bioactive compounds can be challenging because of limitations such as poor solubility, stability, and effective topical delivery. [13]
The proposed formulation combines these components through a single delivery approach:

Curcumin + Tea Tree Oil
↓
Niosomal encapsulation
↓
Optimized niosomal dispersion
↓
Incorporation into Carbopol 934 gel
↓
Enrichment with Aloe vera
↓
Curcumin and Tea Tree Oil-loaded Aloe vera niosomal gel

This approach is intended to combine the biological properties of the selected natural ingredients with the potential delivery advantages of a niosomal system and the practical benefits of a topical gel. [14]

1.9 Aim of the Study

The present study was undertaken to develop and characterize a Curcumin and Tea Tree Oil-loaded niosomal gel enriched with Aloe vera as a potential topical formulation for acne management. The prepared niosomal formulations were evaluated for their physicochemical characteristics, and the optimized formulation was subsequently incorporated into a Carbopol 934 gel base enriched with Aloe vera and evaluated for its suitability as a topical niosomal gel.

1.10 Methods of Preparation of Niosomes

Niosomes can be prepared using several techniques depending on the nature of the drug, desired vesicle size, and intended application. The choice of preparation method influences the vesicle morphology, particle size, entrapment efficiency, and stability of the formulation.[15] The commonly used methods for the preparation of niosomes are:

- Thin Film Hydration Method
- Reverse Phase Evaporation Method
- Proniosome Method
- Bubble Method
- Micro fluidization Method
- Sonication Method [16]

Ether Injection Method

Principle

The **Ether Injection Method** is a simple technique used for the preparation of niosomes based on the rapid evaporation of an organic solvent. In this method, non-ionic surfactants and stearic acid dissolved in diethyl ether are slowly injected into a warm aqueous phase containing the drug. As the ether comes into contact with the heated aqueous medium, it evaporates immediately due to its low boiling point, leading to the self-assembly of surfactant molecules into bilayer vesicles and the formation of niosomes. This method is generally employed to prepare unilamellar vesicles with relatively uniform particle size.[17]

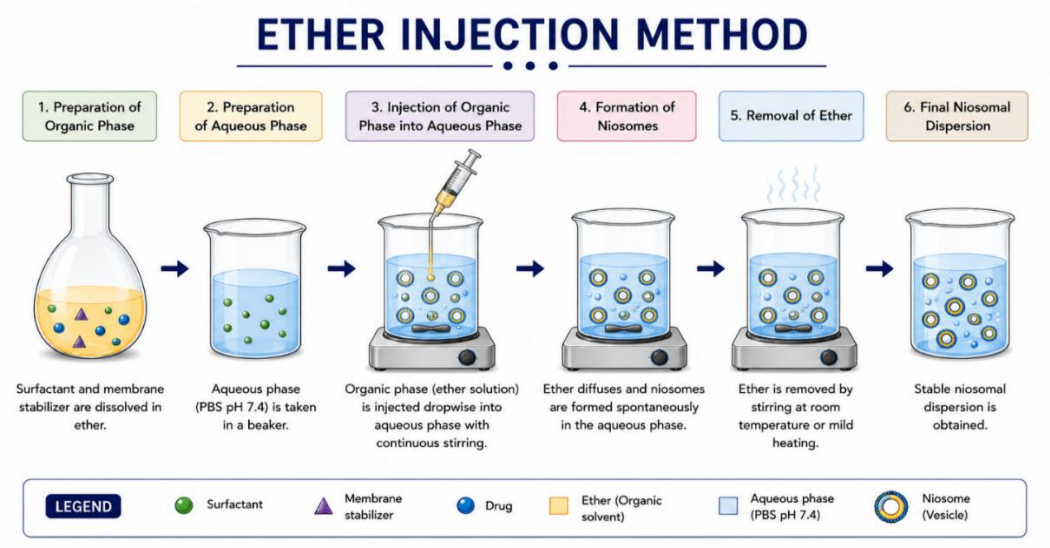


Fig 3: Ether Injection Method

2. MATERIALS AND METHODS

The chemicals that were used are AR/LR grade or the best possible grade available were used as supplied by manufacturer without further purification or investigation.

Chemical's List

Table 1. List of Chemicals

SI.NO	MATERIAL	SOURCE
1.	Curcumin	Otto Chemie Pvt. Ltd
2.	Aloe Vera	Fresh Aloe vera leaves – Local source
3.	Tea tree oil	Raasa Oils,102, Gayatri Vatika, Noida
4.	Span 20	Molychem, Mumbai.
5.	Stearic acid	COBA Chemi Pvt. Ltd
6.	Phosphate Buffer (pH:7.4)	Prepared in laboratory using Analytical Grade chemicals
7.	Diethyl Ether	SDFCL – SD Fine Chemi Ltd, Mumbai
8.	TEA	Thomas Baker Pvt. Ltd, Maharashtra.
9.	Methyl Paraben	Thomas Baker Pvt. Ltd, Maharashtra.
10.	Carbopol 934	Molychem, Mumbai.
11.	Propylene Glycol	Thomas Baker Pvt. Ltd, Maharashtra.
12.	Glycerin	Thomas Baker Pvt. Ltd, Maharashtra.
13.	Distilled Water	Spurthy college of Pharmacy

Equipment's List

Table 2: List of Equipments

S.No	Equipment	Model/ Company
1.	Electronic balance	Systronics, Gujarat
2.	UV spectrophotometer	Jasco Int.co.Ltd, Japan
3.	Centrifuge	Jasco Int.co.Ltd, Japan
4.	Magnetic stirrer	REMI Electrotecnics Ltd, Mumbai, India
5.	Digital pH meter	Aczet Pvt, Ltd
6.	Viscometer	Brookfield DV-II + Pro
7.	Zeta potential analyzer	zetaatrac
8.	Melting point apparatus	S A Instruments & Systems, Thane, Maharashtra
9.	Hot air oven	Balaji Machinery, Faridabad, Haryana
10.	Laboratory Stirrer	REMI Electrotecnics Ltd, Mumbai, India
11.	Desicator	Glassco Laboratory Equipments Pvt. Ltd., Ambala, Haryana
12.	Water Bath	REMI Electrotecnics Ltd, Mumbai, India

2.1 PRE-FORMULATION STUDIES OF CURCUMIN

Pre-formulation studies are the investigations carried out on an active pharmaceutical ingredient (API) before formulation development to determine its physical, chemical, physicochemical, and mechanical properties. These studies help in selecting suitable excipients, manufacturing methods, dosage forms, packaging materials, and storage conditions to ensure the development of a safe, effective, and stable pharmaceutical product.

The objective of pre-formulation studies is to evaluate the physical and chemical properties of a drug before formulation. These studies help in selecting suitable excipients, developing a stable dosage form, and ensuring the quality, safety, and efficacy of the final product.

A. Curcumin

1.Authentication of curcumin

Curcumin was authenticated using the Certificate of Analysis (COA) provided by **Otto Chemie Pvt. Ltd.** The supplied curcumin was identified as Curcumine, 99%, with CAS No. 458-37-7 and molecular weight 368.38 g/mol. The certificate reported an assay of 99.05%, with the sample appearing as an orange solid. The reported melting point was 183–188°C, which complied with the specified standard. The product was supplied under Batch No. 0048 and the certificate stated that the product complied with the prescribed quality standards.

2. Organoleptic Evaluation

Curcumin was examined visually for its colour, appearance, and odour. A small quantity of the sample was placed in a clean, dry glass Petri dish and observed under suitable lighting. The odour was assessed carefully by gently wafting the sample towards the nose without direct inhalation.

3. Solubility Study of Curcumin

The solubility of curcumin was determined qualitatively in different solvents. A known amount of curcumin, such as 10 mg, was transferred separately into test tubes containing 1 mL of different solvents, such as distilled water, chloroform, Di-ethyl ether and phosphate buffer pH 7.4. The samples were shaken thoroughly and observed for dissolution. If necessary, the mixtures were allowed to stand and then examined for undissolved particles.

4. Melting Point Determination

The melting point of curcumin was determined using the capillary tube method. A small quantity of finely powdered curcumin was packed into a clean, dry capillary tube. The capillary was attached to a thermometer and placed in a melting point apparatus containing a suitable heating medium. The sample was heated gradually, and the temperature at which the powder began to melt and the temperature at which it completely melted were recorded.

5. Moisture Content (Loss on Drying)

The moisture content of curcumin was determined by the loss-on-drying method**.** A clean, dry Petri dish was accurately weighed, and the weight was recorded as W_1. Approximately 1 g of curcumin was accurately transferred into the Petri dish, and the combined weight was recorded as W_2. The Petri dish containing the sample was placed in a hot-air oven and dried under the specified conditions until a constant weight was obtained. The dish was then removed from the oven, cooled to room temperature in a desiccator, and weighed accurately. The final weight was recorded as W_3.
The percentage moisture content was calculated using the following equation:

$$\%\ Moisture\ content\ = \frac{W2-W3}{W2-W1} \times 100$$

Where:
W_1 = Weight of empty, dry Petri dish
W_2 = Weight of Petri dish + curcumin before drying
W_3 = Weight of Petri dish + curcumin after drying

6. UV Spectrophotometric Analysis

The maximum absorption wavelength (λmax) of curcumin was determined using a

UV–Visible spectrophotometer. An accurately weighed quantity of curcumin was dissolved in a suitable solvent based on its solubility, and a stock solution of known concentration was prepared. The stock solution was suitably diluted to obtain an appropriate working concentration for spectrophotometric analysis.

The prepared solution was transferred to a quartz cuvette, and the corresponding solvent was used as the blank. The solution was scanned over a wavelength range of 200–600 nm using a UV–Visible spectrophotometer. The wavelength at which curcumin exhibited maximum absorbance was recorded as its λmax.

The experimentally obtained λmax was compared with the reported value and was subsequently used for the quantitative estimation of curcumin in the developed niosomal formulation.

7. Ash value

A known quantity of curcumin sample (approximately 2 g) was accurately weighed and transferred into a previously ignited, cooled and weighed silica crucible. The sample was initially heated gently to remove moisture and volatile matter. It was then incinerated in a muffle furnace at about 600°C until a constant weight of ash was obtained. The crucible was allowed to cool in a desiccator and weighed.

The percentage of total ash was calculated using the following formula:

$$Total\ Ash(\%) = \frac{\text{Weight of Ash}}{\text{Weight of Sample}} \times 100$$

8. Extractive Value Determination of Curcumin

A known quantity (5 g) of curcumin sample was accurately weighed and macerated with 100 mL of the selected solvent in a closed flask for 24 hours, with frequent shaking during the first 6 hours. The mixture was then filtered. A measured quantity of the filtrate was transferred to a previously weighed evaporating dish and evaporated to dryness. The residue was dried to constant weight and weighed. The percentage of extractive value was calculated as:

$$Extractive\ Value\ (\%) = \frac{\text{Weight of sample} \times \text{Volume of filtrate}}{\text{Weight of dried extract} \times \text{Volume of solvent}} \times 100$$

9. Preliminary Phytochemical Screening of Curcumin

Preliminary phytochemical screening of the curcumin sample was carried out to detect the presence of different classes of phytoconstituents. The following qualitative tests were performed:

a. Test for Phenolic Compounds (Ferric chloride test):

A small quantity of Curcumin was dissolved in a suitable solvent and a few drops of ferric chloride solution were added. The development of a brown colour indicated the presence of phenolic compounds.

b. Test for Flavonoids (Shinoda test):

Curcumin was dissolved in a suitable solvent, followed by the addition of a small amount of magnesium turnings and concentrated hydrochloric acid. The development of pink, red, or orange colour indicated the presence of flavonoids.

c. Test for Tannins (Gelatin test):

A solution of Curcumin was treated with 1% gelatin solution containing sodium chloride. Observation of white precipitate indicated the presence of tannins.

d. Test for Alkaloids (Dragendorff's test):

Curcumin was suitably dissolved and treated with Dragendorff's reagent. Development of orange or reddish-brown precipitate indicated the presence of alkaloids.

e. Test for Saponins (Foam test):

Curcumin was mixed with distilled water and shaken vigorously for several minutes.

Observation of persistent froth indicated the presence of saponins.

f. Test for Terpenoids (Salkowski test):

Curcumin was dissolved in chloroform, and concentrated sulfuric acid was carefully added along the side of the test tube. Characteristic reddish-brown colour at the interface indicated the presence of terpenoids.

B. Tea Tree Oil

1. Authentication report of Tea Tree Oil

Tea Tree Oil used in the formulation was procured from **Raasa Oils** and authenticated based on the supplier-provided Certificate of Analysis (CoA). The CoA identified the material as *Melaleuca alternifolia* essential oil and reported its physical appearance, colour, odour, solubility, specific gravity, refractive index, optical rotation and flash point, with the tested parameters reported as complying with the specified ranges.

2. Organoleptic Evaluation

Tea Tree Oil was examined visually for its colour, appearance, and odour. A small quantity of the sample was placed in a clean, dry glass Petri dish and observed under suitable lighting. The odour was assessed carefully by gently wafting the sample towards the nose without direct inhalation.

3. Solubility Study

The solubility of Tea Tree Oil was determined qualitatively in selective solvents. Approximately 0.1 mL of tea tree oil was added separately to 1 mL of distilled water, phosphate buffer pH 7.4, and diethyl ether. Each mixture was shaken thoroughly and observed for complete mixing, dispersion, or phase separation.

4. Specific Gravity

The specific gravity of tea tree oil was determined using a calibrated specific gravity bottle (pycnometer). The clean, dry, and empty bottle was accurately weighed, and the weight was recorded as W_1. The bottle was then filled completely with distilled water, ensuring the absence of air bubbles, and fitted with its stopper. The external surface of the bottle was dried carefully, and the bottle was weighed accurately. The weight was recorded as W_2.

The bottle was subsequently emptied, cleaned, and dried thoroughly. It was then filled completely with tea tree oil under the same experimental conditions and fitted with the stopper. The outside of the bottle was wiped dry, and the bottle containing tea tree oil was accurately weighed. The weight was recorded as W_3.

The specific gravity of tea tree oil was calculated using the following equation:

$$Specific\ Gravity = \frac{W3 - W1}{W2 - W1}$$

Where:

W_1 = Weight of the empty specific gravity bottle

W_2 = Weight of the bottle filled with distilled water

W_3 = Weight of the bottle filled with tea tree oil

5. UV-Spectrometric Analysis

Tea Tree Oil was diluted with ethanol to prepare a suitable sample solution. The UV–Visible spectrophotometer was calibrated using ethanol as the blank. The prepared Tea Tree Oil solution was transferred into a quartz cuvette and scanned over the wavelength range of 200–400 nm. The absorbance spectrum was recorded, and the wavelength corresponding to maximum absorbance (λmax) was determined from the obtained spectrum.

6. Partition Coefficient Determination of Tea Tree Oil

The apparent partition coefficient of tea tree oil was determined by the shake-flask method using a gravimetric approach, with ethyl acetate as the organic phase and phosphate buffer pH 7.4 as the aqueous phase. About 1 mL of tea tree oil was accurately measured and transferred into a separating funnel containing 10 mL of ethyl acetate and 10 mL of phosphate buffer pH 7.4. The mixture was shaken gently for 10–15 minutes and allowed to stand until complete separation of the two phases. The upper ethyl acetate layer and lower aqueous layer were separated carefully.

A clean, dry evaporating dish was accurately weighed and recorded as W_1. The separated ethyl acetate phase was transferred into the dish and the solvent was allowed to evaporate completely. After cooling in a desiccator, the dish was weighed and recorded as W_2. The amount of tea tree oil recovered in the organic phase was calculated as $\boldsymbol{W_2 - W_1}$.

The aqueous phase was extracted with fresh ethyl acetate in three successive portions. The combined extracts were transferred to another pre-weighed evaporating dish, and the solvent was evaporated completely. The dish was cooled and weighed as W_4, while the empty dish weight was recorded as W_3. The amount of tea tree oil recovered from the aqueous phase was calculated as $\boldsymbol{W_4 - W_3}$.

Calculate the partition coefficient using:

$$P = \frac{\mathrm{Ca}}{\mathrm{Co}}$$

Where:

- Ca = concentration of Tea Tree Oil in the Organic phase
- Co = concentration of Tea Tree Oil in the aqueous phase

7. Preliminary phytochemical screening

Preliminary phytochemical screening of the Tea Tree Oil sample was carried out to detect the presence of different classes of phytoconstituents. The following qualitative tests were performed:

a. Test for Terpenoids (Salkowski test):

Tea Tree Oil was mixed with chloroform and concentrated sulfuric acid was carefully added along the side of the test tube. The formation of a reddish-brown colour at the interface indicated the presence of terpenoids.

b. Test for Steroids (Liebermann–Burchard test):

Tea Tree Oil was dissolved in chloroform, followed by the addition of acetic anhydride. Concentrated sulfuric acid was then added carefully along the side of the test tube. The development of a green or bluish-green colour indicated the presence of steroids.

c. Test for Phenolic Compounds (Ferric chloride test):

A small quantity of Tea Tree Oil was diluted with a suitable solvent and a few drops of ferric chloride solution were added. The development of a blue, green, or violet colour indicated the presence of phenolic compounds.

d. Test for Flavonoids (Shinoda test):

Tea Tree Oil was diluted with a suitable solvent, followed by the addition of a small amount of magnesium turnings and concentrated hydrochloric acid. The development of a pink, red, or orange colour indicated the presence of flavonoids.

e. Test for Tannins (Ferric chloride test):

A diluted Tea Tree Oil sample was treated with a few drops of ferric chloride solution. The development of a blue-black or green colour indicated the presence of tannins.

f. Test for Saponins (Foam test):

Tea Tree Oil was mixed with distilled water and shaken vigorously for several minutes. The formation of persistent froth indicated the presence of saponins.

h. Test for Alkaloids (Dragendorff's test):

Tea Tree Oil was suitably diluted and treated with Dragendorff's reagent. The formation of an orange or reddish-brown precipitate indicated the presence of alkaloids.

2.2 Preparation of Curcumin, Tea Tree Oil - Loaded Niosome [CTT-N]

Formulation Code for Curcumin, Tea Tree Oil loaded Niosome

Table 3: Formulation Chart for Curcumin, Tea Tree Oil loaded Niosome

INGREDIENTS	F1	F2	F3	F4
Curcumin	0.025 g	0.025 g	0.025 g	0.025 g
Tea Tree Oil	0.5 mL	0.5 mL	0.5 mL	0.5 mL
Span 20	0.1 g	0.15 g	0.2 g	0.25 g
Stearic Acid	0.05 g	0.075 g	0.1 g	0.125 g
Phosphate Buffer pH: 7.4	10 mL	10 mL	10 mL	10 mL
Diethyl Ether	10 mL	10 mL	10 mL	10 mL

1. Preparation of phosphate Buffer pH: 7.4

Sodium dihydrogen phosphate - 0.31 g
↓
Dissolve in a suitable quantity of distilled water
↓
Add Disodium hydrogen phosphate - 1.09 g
↓
Mix thoroughly until completely dissolved
↓
Make up the volume to 100 mL with distilled water
↓
Calibrate the pH meter
↓
Measure the pH of the prepared buffer
↓
Adjust to pH 7.4 if required
(NaOH to increase pH, HCl to decrease pH)
↓
Phosphate Buffer pH 7.4

2. Preparation of Turmeric – Tea Tree Oil loaded Niosome

Materials:

1. Curcumin
2. Tea Tree Oil
3. Span 20
4. Stearic Acid
5. Phosphate Buffer Ph:7.4
6. Diethyl Ether

Procedure:

Preparation of CTT-N for F3 by Ether injection Method

1. Preparation of organic phase

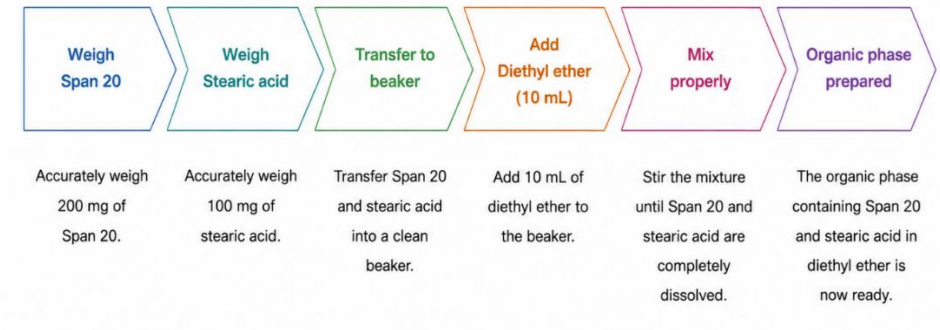


Fig 4: Preparation of Organic Phase

Span 20 (0.2 g) + Stearic acid (0.1 g)
↓
Accurately weigh and transfer into a clean container
↓
Add Diethyl ether (10 mL)
↓
Mix continuously until a uniform solution is obtained
↓
Add Curcumin (0.025 g)
↓
Add Tea tree oil (0.5 mL)
↓
Mix thoroughly for uniform distribution
↓
Organic phase obtained
↓
Ready for Ether Injection Method

2. Preparation of Aqueous Phase

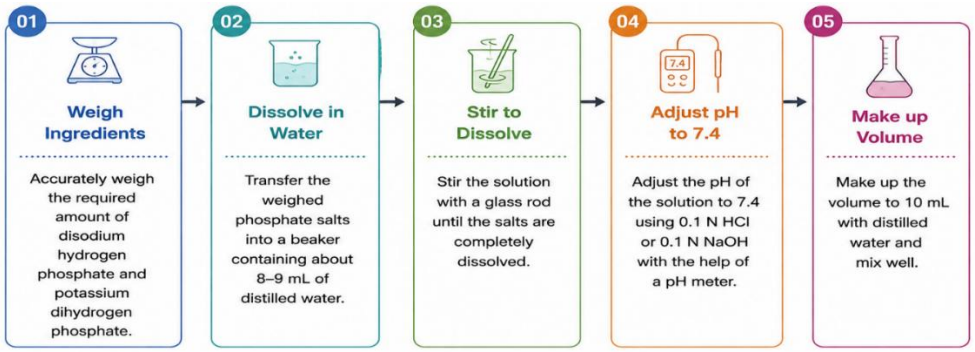


Fig 5: Preparation of aqueous Phase

Phosphate buffer pH 7.4 (10 mL)
↓
Transfer into a suitable vessel
↓
Heat the buffer to 55–65°C
↓
Maintain at 55–65°C with continuous stirring
↓
Slowly add the prepared organic phase
↓
Diethyl ether evaporates rapidly due to elevated temperature
↓
Continuous stirring promotes vesicle formation
↓
Curcumin–Tea Tree Oil-loaded niosomal dispersion obtained

3. Ether Injection

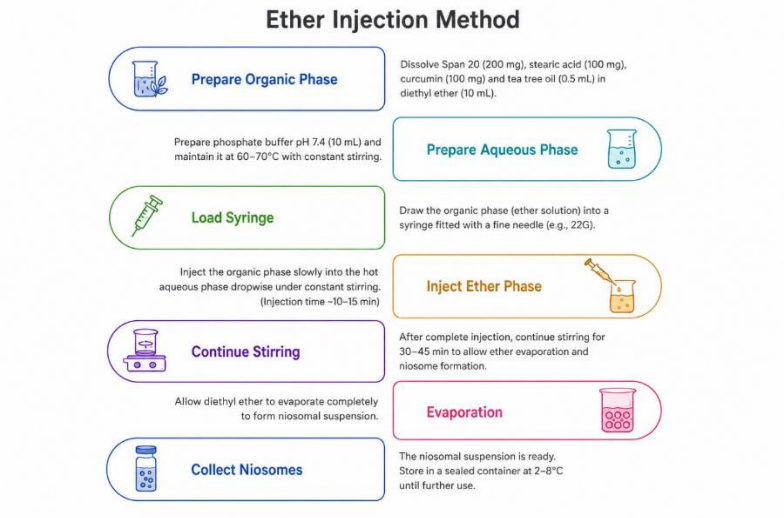


Fig 6: Ether Injection Method

Prepared organic phase
(Span 20 + Stearic acid + Curcumin + Tea tree oil + Diethyl ether)
↓
Transfer the organic phase into a suitable syringe
↓
Heat phosphate buffer pH 7.4 to 55–65°C
↓
Slowly inject the organic phase through a syringe and needle
↓
Maintain continuous stirring during injection
↓
Ensure gradual and uniform dispersion of the organic phase
↓
Rapid evaporation of diethyl ether due to elevated temperature
↓
Continued stirring promotes vesicle formation
↓
Curcumin–Tea Tree Oil-loaded niosomal vesicles obtained

4. Formation of Curcumin–Tea Tree Oil-Loaded Niosomes

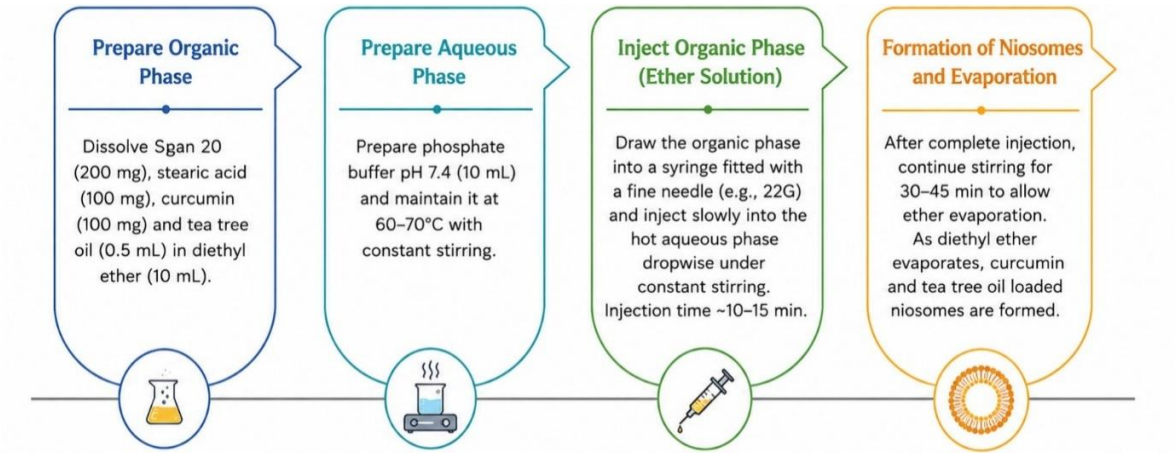


Fig 7: Formation of CTT-N

Diethyl ether evaporates rapidly during injection
↓
Span 20 and stearic acid arrange at the interface
↓
Formation of vesicular structures
↓
Curcumin–Tea Tree Oil-loaded niosomes formed
↓
Continue stirring for 30–45 minutes
↓
Removal of residual diethyl ether and completion of vesicle formation
↓
Cool the niosomal dispersion to room temperature
↓
Collect the prepared niosomal dispersion
↓
Store appropriately for further evaluation

2.3 Evaluation of niosome

1. Appearance

The prepared niosomal formulation was visually examined for its colour, odour, texture, clarity, and physical appearance. The formulation was also checked for the presence of any lumps, aggregates, precipitation, or phase separation. A uniform appearance indicates proper distribution of the formulation components.

2. Homogeneity

The homogeneity of the prepared formulation was evaluated by taking a small quantity of the formulation and examining it visually and by gently spreading it on a glass slide. The formulation was checked for uniform distribution of ingredients, absence of lumps, aggregates, and foreign particles. A homogeneous formulation indicates good uniformity and consistency.

3. pH

The pH of the prepared formulation was determined using a previously calibrated digital pH meter. A suitable quantity of the formulation was placed in a clean beaker, and the electrode was immersed into the sample. The pH was recorded after obtaining a stable reading. The pH was maintained within a range suitable for topical application and skin compatibility.

4. Particle Size

The particle size of the prepared niosomes was determined to evaluate the size and uniformity of the vesicles. The niosomal dispersion was suitably diluted and analyzed using dynamic light scattering (DLS). The average particle size and particle-size distribution were recorded. Smaller and relatively uniform vesicles may provide better distribution and interaction with the skin.

5. Zeta Potential

The zeta potential of the prepared niosomes was determined using a zeta potential analyzer. The sample was suitably diluted and introduced into the instrument for measurement. Zeta potential indicates the surface charge of the vesicles and provides information regarding the physical stability of the niosomal dispersion. A higher absolute zeta-potential value generally indicates better electrostatic repulsion between vesicles and reduced aggregation.

6. Drug Entrapment Efficiency

The entrapment efficiency was determined to evaluate the percentage of curcumin successfully incorporated into the niosomal vesicles. A known quantity of niosomal dispersion was centrifuged to separate the niosomal vesicles from the free or unentrapped drug. The supernatant containing the free drug was separated carefully, and the amount

of free curcumin was quantified using a suitable analytical method.

The percentage entrapment efficiency was calculated using:

$$Entrapment\ Efficacy = \frac{\text{Total Drug} - \text{Free (unentrapped drug)}}{\text{Total Drug}} \times 100$$

7. Drug Content

Drug content analysis was performed to determine the amount of curcumin present in the prepared niosomal formulation. A known quantity of formulation was accurately weighed and treated with a suitable solvent to extract the drug. The extract was filtered and analyzed using an appropriate quantitative analytical technique. The obtained drug concentration was compared with the theoretical drug concentration, and the percentage drug content was calculated.

$$Drug\ Content\ (\%) = \frac{\text{Actual amount of drug present}}{Theorital\ amount\ of\ drug} \times 100$$

2.4 Preparation of niosomal gel

Materials:

1. Curcumin–tea tree oil-loaded niosomal dispersion
2. Carbopol 934
3. Aloe vera gel
4. Propylene glycol
5. Glycerin
6. Triethanolamine
7. Methyl paraben
8. Distilled water

Formulation Code for log batch of Niosomal Gel

Table 4: Formulation Chart for Curcumin, Tea Tree Oil loaded Niosomal gel

FORMULATION CODE	G1	G2	G3
Niosomal Suspension	2 mL of CTT-N	2 mL of CTT-N	2 mL of CTT-N
Carbopol 934	0.5 g	0.75 g	1 g
Triethanol Amine	q.s	q.s	q.s
Glycerin	2 mL	2 mL	2 mL
Aloe vera gel	5 g	5 g	5 g
Propylene Glycol	2 mL	2 mL	2 mL
Methyl Paraben	0.01 g	0.01 g	0.01 g
Distilled Water	q.s	q.s	q.s

1. Hydrate Carbopol for Gel Base

Carbopol 934 – 1 g

↓

Accurately weigh Carbopol 934

↓

Slowly disperse in the required quantity of distilled water

↓

Continuous gentle stirring

↓

Allow to stand for 12–24 hours at room temperature

↓

Complete hydration and swelling of Carbopol particles

↓

Smooth and uniform Carbopol dispersion is obtained

↓

Gel Base

2. Addition of Formulation Ingredients

Hydrated Carbopol 934 gel base
↓
Add Aloe vera gel extract – 5 g
↓
Mix gently until uniformly distributed
↓
Add Propylene glycol – 2 mL
↓
Add Glycerin – 2 mL
↓
Add Methyl paraben – 0.01 g
(dissolved in a small quantity of propylene glycol before addition)
↓
Mix thoroughly to obtain a uniform gel base
↓
Add Triethanolamine (TEA) dropwise
↓
Adjust pH to approximately 5.5–6.0
↓
Smooth and uniform aloe vera gel base obtained

3. Incorporation of Niosomal Dispersion

Prepared curcumin–tea tree oil-loaded niosomal dispersion
↓
Slowly add the niosomal dispersion to the hydrated Carbopol gel base
↓
Add gradually with gentle and continuous stirring
↓
Ensure uniform distribution of niosomes throughout the gel base
↓
Avoid vigorous stirring to minimize vesicle aggregation or damage
↓
Continue gentle stirring until uniformly mixed
↓
Smooth and homogeneous niosomal gel obtained

2.5 Evaluation of niosomal gel

1. Appearance

The prepared niosomal gel was visually examined for colour, odour, texture, clarity, and consistency. The formulation was also checked for the presence of lumps, aggregates, air bubbles, precipitation, or phase separation. A smooth and uniform appearance indicates good physical characteristics of the formulation.

2. Homogeneity

The homogeneity of the prepared gel was evaluated by placing a small quantity of formulation on a clean glass slide and examining it visually. The gel was checked for uniform distribution of ingredients, absence of lumps, aggregates, and foreign particles. The formulation should show a smooth and uniform texture without any visible separation.

3. pH

The pH of the prepared niosomal gel was determined using a calibrated digital pH meter. A suitable quantity of gel was dispersed in distilled water and the electrode was immersed into the sample. The pH was recorded after obtaining a stable reading.
The pH of a topical formulation should preferably be maintained around 5.5–6.5 for better skin compatibility.

4. Viscosity

The viscosity of the prepared niosomal gel was determined using a Brookfield viscometer. An appropriate spindle, such as L4, was selected according to the consistency of the formulation. The viscosity was measured at a predetermined rotational speed and at room temperature. The reading was recorded in centipoise (cP).

5. Spreadability

Spreadability was determined to evaluate the ease with which the niosomal gel spreads over the skin. A known quantity of gel was placed between two clean glass slides. A specified weight was placed on the upper slide, and the time required for the gel to spread over a specified distance was recorded.
The spreadability can be calculated using:

$$S = \frac{M \times L}{T}$$

Where:
S = Spreadability (g·cm/sec)
M = Weight applied to the upper slide (g)
L = Length travelled by the gel (cm)
T = Time taken (sec)

6. Extrudability

Extrudability was evaluated to determine the ease with which the niosomal gel can be removed from a collapsible tube. A known quantity of gel was filled into the tube and the tube was properly closed. A specified weight was applied to the tube, and the amount of gel extruded through the nozzle was measured.
Extrudability can be expressed as:

$$E = \frac{W}{L}$$

Where:
E = Extrudability (g/cm)
W = Weight of gel extruded (g)
L = Length of gel extruded (cm)

7. Drug Content

Drug content was determined to evaluate the amount of curcumin present in the prepared niosomal gel. A known quantity of gel was accurately weighed and treated with a suitable solvent to extract the curcumin. The mixture was properly mixed and filtered to remove the gel components. The drug concentration was then determined using a suitable quantitative analytical method such as UV-Visible spectroscopy or HPLC.
The percentage drug content was calculated using:

$$Drug\ Content\ \% = \frac{\text{Actual amount of drug present}}{\text{Theroretical amount of drug}} \times 100$$

3. RESULT

3.1 Pre formulation studies

A. Pre formulation studies of Curcumin

1. Authentication of curcumin

The procured Curcumin was authenticated by the supplier/manufacturer and the authentication Certificate of Analysis was obtained. The report confirmed the identity and quality of Curcumin used for the formulation studies. The sample was reported to have 99% purity and was considered suitable for further preformulation and formulation studies.

Otto Chemie Pvt. Ltd.

An ISO 9001 : 2015 & GMP Certified Company
Web : www.ottokemi.com Email : info@ottokemi.com

Curcumine, 99%

Product Code: C 2735

PROPERTIES	
CAS	458-37-7
Synonyms	(E,E)-1,7-bis(4-Hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione, Diferuloylmethane, Diferulylmethane, Natural Yellow 3
Chemical Formula	$C_{21}H_{20}O_6$
Molecular Weight	368.38
Packing	Bottle / Drum
Batch No.	0048
Mfg. Date	11-Jun-2025
Retest Date	11-Jun-2030

TEST	SPECIFICATIONS	RESULTS
Assay	99%+	99.05%
Appearance (Form)	Solid	Complies
Appearance (Colour)	Orange	Orange
Melting point	183-188 °C	Complies
Colour Index Number	75300	75300

The product complies with the prescribed standards of quality

This document has been produced electronically and it is valid without signature.

The above particulars do not release the customer from the obligation to carry out an inspection of goods received. Not for medicinal use. Please test before use.

HO Add.: No 603, 6th Floor, 87, Tardeo Road, Mumbai- 400 034, Maharashtra, India (Bharat).
Works : 101, Aarkay Ruby Industrial Estate(1B), Opp Shree Narayan Industrial Estate, Chinchpada, Vasai East, Waliv, Maharashtra 401208, India (Bharat).
Email : qc@ottokemi.com Contact no.: +91 98200 41841

Fig 8: Authentication Certificate of Analysis of Curcumin

2. Determination of Organoleptic characters

The Organoleptic characters like colour, Odour and state for the given drug sample was studied.

Table 5: Organoleptic test of Curcumin

Colour	Orange
Appearance	Solid (powder)
Odour	Visually odourless
Texture	Fine Powder

3. Determination of Solubility

Table 6: Solubility profile of Curcumin

Medium	Solubility
Water	Insoluble
Diethyl Ether	Soluble
Phosphate buffer Ph:7.4	Partially Insolube

4. Determination of Melting point

Table 7: Melting point of Curcumin

Drug Name	Observed Melting point	Standard Melting point
Curcumin	185°C	183–188 °C

5. Moisture Content (Loss on Drying)

Table 8: Determination of Moisture Content of Curcumin

Parameter	Observation
W_1 = Weight of empty Petri Dish	28.65 g
W_2 = Empty Petri Dish + curcumin before drying	29.15 g
W_3 = Weight of Petri Dish + curcumin after drying	29.14 g
Moisture Content	2.0 %

6. UV Spectrophotometric Analysis

Table 9: λmax of Curcumin

Drug Name	Observed λmax (nm)	Standard λmax (nm)
Curcumin	425 nm	421 nm-425 nm

7. Ash Value

Table 10: Determination of Ash Value of Curcumin

Parameter	Observation
Weight of empty crucible	30.000 g
Weight of curcumin sample	2.000 g
Weight of crucible + ash	30.020 g
Weight of ash	0.020 g
Ash value	1.0% w/w

Weight of ash = 30.020 − 30.000 = 0.020g

$$Ash\ value = \frac{0.020}{2.000} \times 100$$

Ash value=1.0

8. Extractive Value Determination of Curcumin

$$Extractive\ Value\ \% = \frac{4.2}{5} \times 100$$

Extractive value =84%

Table 11: Determination of Extractive Value of Curcumin

Parameter	Observation
Weight of sample	5.0 g
Weight of dried extract	4.2 g
Extractive value	84% w/w

9. Preliminary phytochemical screening

Fig 9: Preliminary Phytochemical Screening of Curcumin

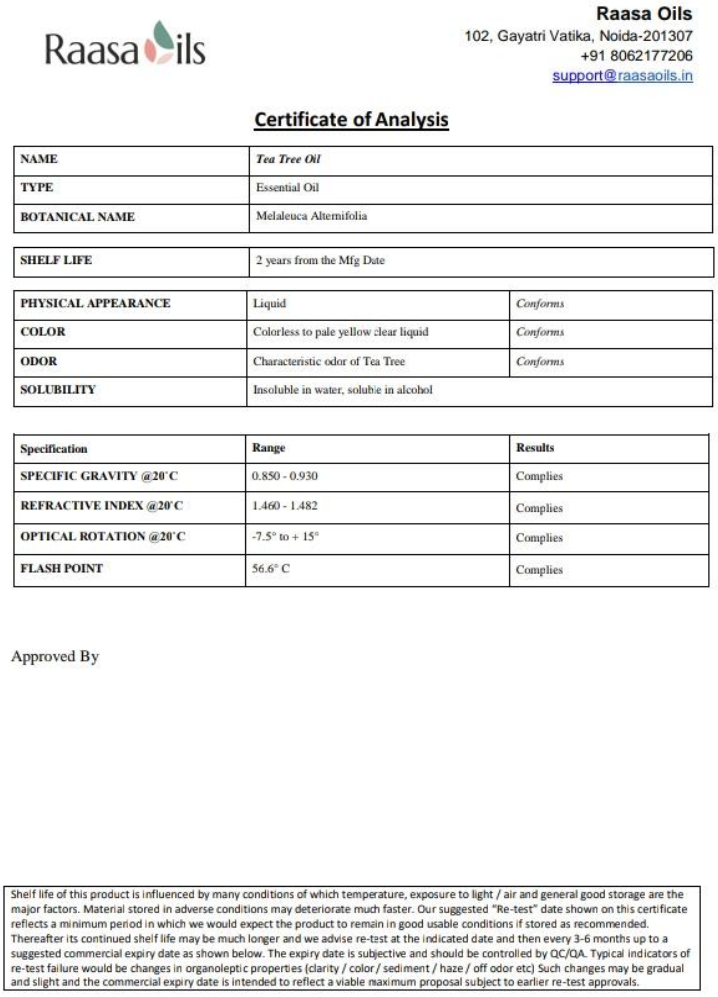
Table 12: Results of Preliminary Phytochemical Screening of Curcumin

S.No	Phytochemical	Test	Observation	Inference
1.	Phenols	Ferric Chloride Test	Blue/Green/violet/brown colour develops	Phenols Present
2.	Flavonoids	Shinoda Test	No characteristic pink/ Red/Orange Colour	Flavonoids Absent
3.	Tannins	Gelatin Test	No White precipitate	Tannins Absent
4.	Alkaloids	Dragendorff's Test	No orange/reddish brown precipitate	Alkaloids Absent
5.	Saponins	Foam Test	No persistant foam	Saponins Absent
6.	Terpenoids	Salkowski Test	No reddish – brown colour at interface	Terpenoid Absent

B. Tea Tree Oil

1. Authentication report of Tea Tree Oil

The procured Tea Tree Oil was authenticated using the Certificate of Analysis (COA) provided by the supplier. The certificate confirmed the identity and quality of the Tea Tree Oil. The major constituents were reported to be terpinen-4-ol (35–48%), γ-terpinene (14–28%) and α-terpinene (6–12%), confirming the characteristic composition of Tea Tree Oil. The sample was considered suitable for further formulation studies.



Raasa Oils
102, Gayatri Vatika, Noida-201307
+91 8062177206
support@raasaoils.in

Certificate of Analysis

NAME	***Tea Tree Oil***
TYPE	Essential Oil
BOTANICAL NAME	Melaleuca Alternifolia

SHELF LIFE	2 years from the Mfg Date

PHYSICAL APPEARANCE	Liquid	*Conforms*
COLOR	Colorless to pale yellow clear liquid	*Conforms*
ODOR	Characteristic odor of Tea Tree	*Conforms*
SOLUBILITY	Insoluble in water, soluble in alcohol	

Specification	**Range**	**Results**
SPECIFIC GRAVITY @20°C	0.850 - 0.930	Complies
REFRACTIVE INDEX @20°C	1.460 - 1.482	Complies
OPTICAL ROTATION @20°C	-7.5° to + 15°	Complies
FLASH POINT	56.6° C	Complies

Approved By

Shelf life of this product is influenced by many conditions of which temperature, exposure to light / air and general good storage are the major factors. Material stored in adverse conditions may deteriorate much faster. Our suggested "Re-test" date shown on this certificate reflects a minimum period in which we would expect the product to remain in good usable conditions if stored as recommended. Thereafter its continued shelf life may be much longer and we advise re-test at the indicated date and then every 3-6 months up to a suggested commercial expiry date as shown below. The expiry date is subjective and should be controlled by QC/QA. Typical indicators of re-test failure would be changes in organoleptic properties (clarity / color / sediment / haze / off odor etc) Such changes may be gradual and slight and the commercial expiry date is intended to reflect a viable maximum proposal subject to earlier re-test approvals.

Fig 10: Authentication Certificate of Analysis of Tea Tree Oil

2. Organoleptic Evaluation

Table 13: Organoleptic test of Tea Tree Oil

Colour	Colourless
Appearance	Clear Liquid
Odour	Strong Characteristic Odour

3. Solubility Study

Table 14: Solubility profile of Tea Tree Oil

Medium	Solubility
Water	Insoluble forms a sperate layer
Diethyl Ether	Soluble
Phosphate buffer Ph:7.4	Partially Insolube

4. Specific Gravity

Table 15: Determination of Specific Gravity of Tea Tree Oil

Parameter	Observation
W1 - Weight of empty bottle	25.63 g
W2 - Weight of bottle + Water	52.32 g
W3 – Weight of bottle + Tea Tree Oil	49.30 g
W2 – W1	26.69 g
W3 – W1	23.67 g
Specific Gravity	0.8868

5. UV-Spectrometric Analysis

Table 16: λmax of Tea Tree Oil

Drug Name	Observed λmax (nm)
Tea Tree Oil	267 nm

7. Partition Coefficient Determination of Tea Tree Oil

Table 17: Determination of Partition Coefficient of Tea Tree Oil

Parameter	Observation
W_1 – Weight of empty evaporating dish (organic phase)	96.57 g
W_2 – Weight of dish + recovered oil (organic phase)	97.18 g
W_3 – Weight of empty evaporating dish (aqueous phase)	79.05 g
W_4 – Weight of dish + recovered oil (aqueous phase)	79.15 g
C_a – Amount of Tea Tree Oil in organic phase	0.61 g
C_o – Amount of Tea Tree Oil in aqueous phase	0.10 g
Partition coefficient of Tea Tree Oil between the organic phase and aqueous phase	6.1

7. Preliminary phytochemical screening

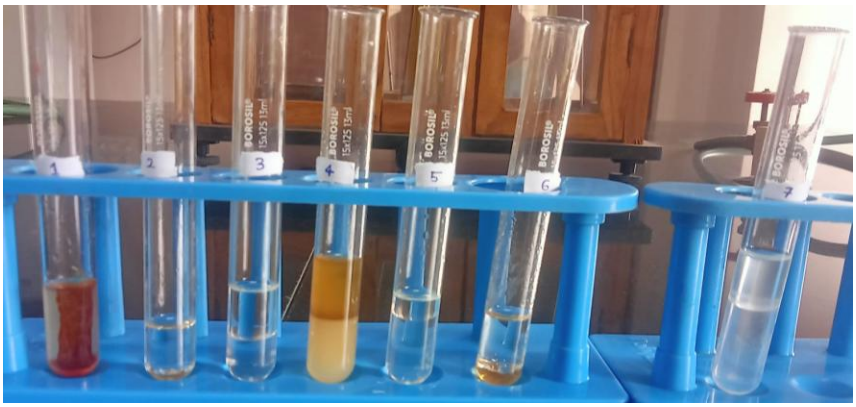


Fig 11: Preliminary Phytochemical Screening of Tea Tree Oil

Table 18: Results of Preliminary Phytochemical Screening of Tea Tree Oil

S.No	Phytochemical	Test	Observation	Inference
1.	Terpenoids	Salkowski test	Reddish-brown colour develops at the interface	Terpenoids Present
2.	Steroids	Liebermann–Burchard test	No green/bluish-green colour develops	Steroids Absent
3.	Phenols	Ferric chloride test	No blue/green/violet colour develops	Phenols Absent
4.	Flavonoids	Shinoda test	No characteristic pink/red/orange colour develops.	Flavonoids Absent
5.	Tannins	Ferric chloride test	No blue-black/green colour develops	Tannins Absent
6.	Saponins	Foam test	No persistent foam develops	Saponins Absent
7.	Alkaloids	Dragendorff's test	No orange/reddish-brown precipitate.	Alkaloids Absent

3.2 Evaluation of niosomes

1. Appearance

Table 19: Appearance of the Prepared Niosomal Formulations (F1–F4)

Parameter	F1	F2	F3	F4
Colour	Yellowish-green	Yellowish-green	**Yellowish-green**	Yellowish-green
Odour	Characteristic odour of tea tree oil	Characteristic odour of tea tree oil	**Characteristic odour of tea tree oil**	Characteristic odour of tea tree oil
Texture	Smooth	Smooth	**Smooth and uniform**	Smooth

Clarity	Uniform	Uniform	**Uniform**	Uniform
Homogeneity	Homogeneous	Homogeneous	**Homogeneous**	Homogeneous
Lumps/Aggregates	Absent	Absent	**Absent**	Absent
Precipitation	Absent	Absent	**Absent**	Absent
Phase separation	Absent	Absent	**Absent**	Absent

Fig 12: Prepared Niosomal Formulations (F1–F4)

2. Homogeneity

Table 20: Homogeneity of the Prepared Niosomal Formulations (F1–F4)

Parameter	F1	F2	F3	F4
Uniform distribution	Good	Good	**Excellent**	Good
Lumps/Aggregates	Absent	Absent	**Absent**	Absent
Foreign particles	Absent	Absent	**Absent**	Absent
Consistency	Uniform	Uniform	**Highly uniform**	Uniform
Overall homogeneity	Good	Good	**Excellent**	Good

3. pH

Table 21: pH of the Prepared Niosomal Formulations (F1–F4)

Formulation	pH
F1	6.2
F2	6.3

F3	6.4
F4	6.5

4. Particle Size

Table 22: Particle Size of Optimized Niosomal Formulation (F3)

Formulation code	Particle Size
F3	286 nm

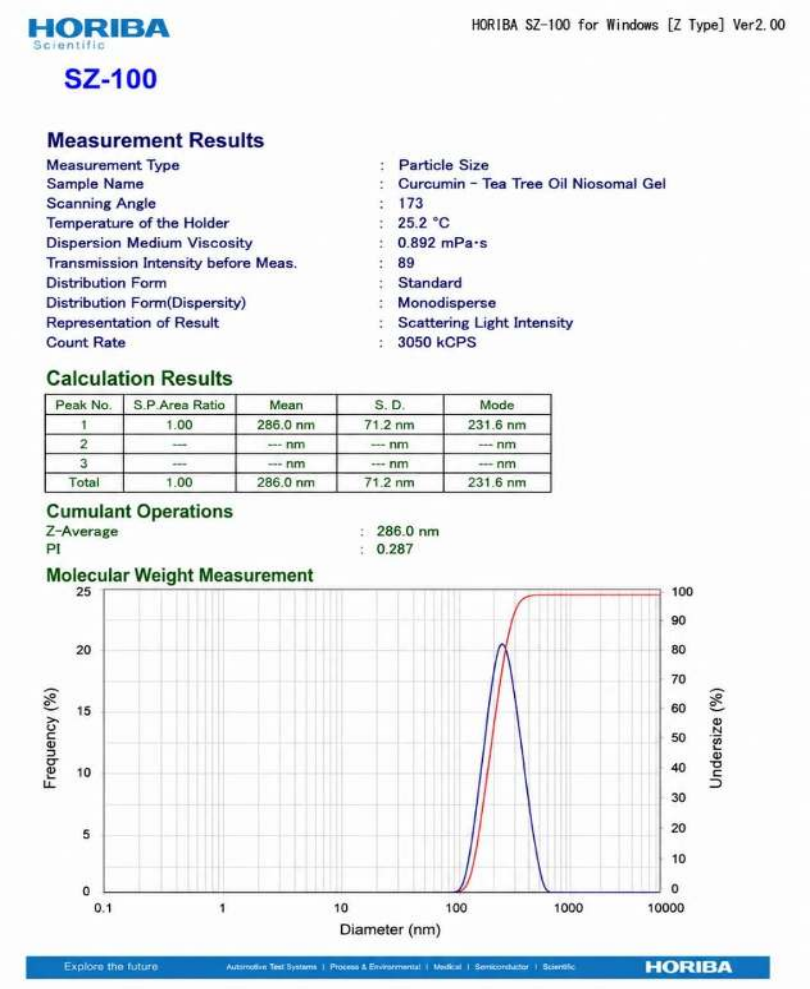


Fig 13: Particle Size Analysis of F3 Niosomal Formulation

5. Zeta Potential

Table 23: Zeta Potential of Optimized Niosomal Formulation (F3)

Formulation Code	Zeta Potential
F3	- 32.4 mV

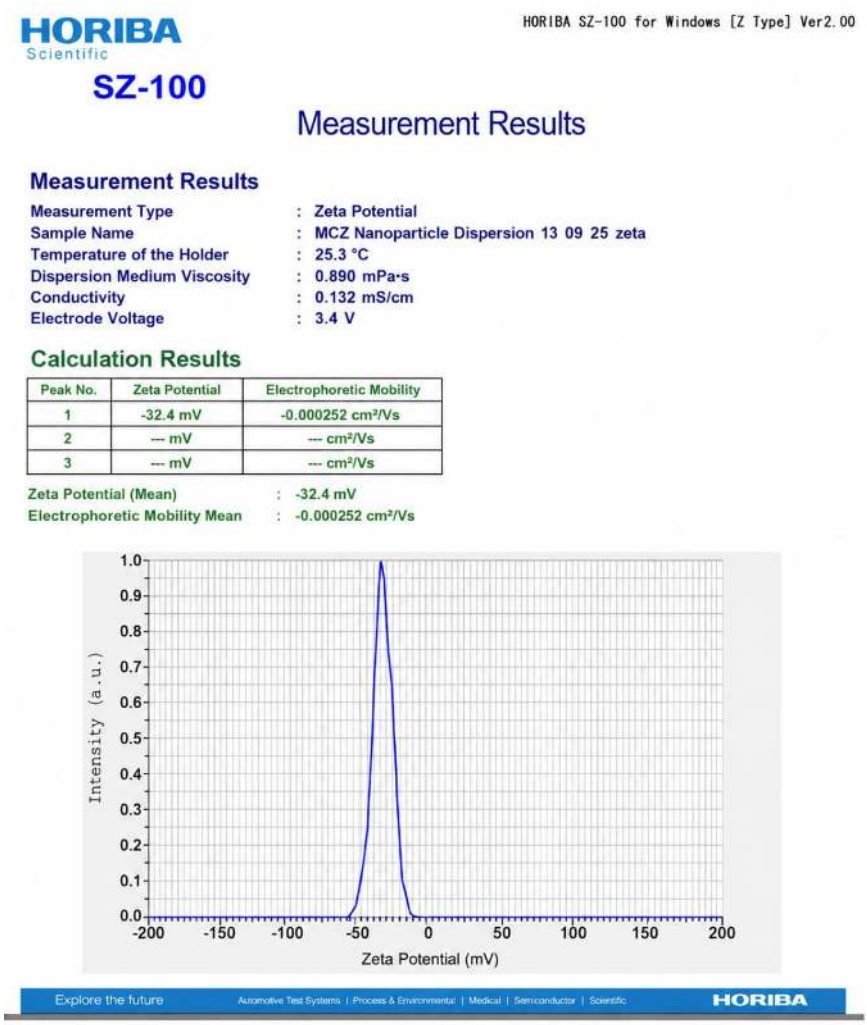


Fig 14: Zeta Potential of F3 Niosomal Formulation

6. Drug Entrapment Efficacy

Table 24: Entrapment Efficiency of the Prepared Niosomal Formulations (F1–F4)

SI.NO	Formulation Code	Percentage Entrapment Efficacy (%)
1.	F1	72.4 %
2.	F2	78.6 %
3.	F3	84.7 %
4.	F4	81.3 %

8. Drug Content

Table 25: Drug Content of the Prepared Niosomal Formulations (F1–F4)

Formulation	Drug Content (%)
F1	94.2
F2	95.6
F3	97.1
F4	96.8

3.3 Evaluation of niosomal gel

1.Appearance

Table 26: Appearance of the Prepared Niosomal Gel Formulations (G1-G3)

Parameter	G1	G2	G3
Colour	Yellowish	Yellowish	Yellowish
Odour	Characteristic	Characteristic	Characteristic
Texture	Smooth	Smooth	Smooth
Consistency	Uniform	Uniform	Uniform
Phase separation	Absent	Absent	Absent

2. Homogeneity

Table 27: Homogeneity of the Prepared Niosomal Gel Formulations (G1–G3)

Parameter	G1	G2	G3
Uniformity	Good	Good	Good
Lumps/Aggregates	Absent	Absent	Absent
Foreign Particles	Absent	Absent	Absent
Phase separation	Absent	Absent	Absent

3. pH

Table 28: pH of the Prepared Niosomal Gel Formulations (G1–G3)

Formulation	pH
G1	5.42
G2	5.48
G3	5.55

Fig 15: pH of Optimized Niosomal Gel Formulation (G3)

4. Viscosity

Table 29: Viscosity of the Prepared Niosomal Gel Formulations (G1–G3)

Formulation	Viscosity (cP)
G1	8420
G2	9180
G3	10308

Fig 16: Viscosity of G3 Niosomal Gel Formulation

5. Spreadability

Table 30: Spreadability of Optimized Niosomal Gel Formulation (G3)

Applied weight (M)	Distance (L)	Time (T)	Spreadability (g.cm/sec)
6 g	1.4 cm	60 sec	0.14
50 g	1.5 cm	60 sec	1.25
100 g	1.9 cm	60 sec	3.17
150 g	2.5 cm	60 sec	6.25

6. Extrudability

Table 31: Extrudability of the Prepared Niosomal Gel Formulations (G1–G3)

Formulation	Gel extruded (g)	Time (sec)	Extrudability (g/sec)
G1	0.80	10	0.080
G2	0.85	10	0.085
G3	0.90	10	0.090

7. Drug Content

Table 32: Drug Content of Niosomal Gel Formulations (G1–G3)

Formulation	Drug content (%)
G1	94.26
G2	96.18
G3	98.42

DISCUSSION

The present study was carried out to develop a Curcumin and Tea Tree Oil-loaded niosomal gel enriched with Aloe vera as a potential topical formulation for acne management. The formulation approach combined the selected natural active ingredients with a niosomal delivery system and an Aloe vera-enriched Carbopol 934 gel base.

The preformulation studies provided preliminary information regarding the physicochemical characteristics of Curcumin and Tea Tree Oil and supported their selection for formulation development. Curcumin showed an orange-coloured, odourless solid nature, while its observed melting point was 185°C and the λmax was 425 nm. The moisture content and ash value were found to be 2.0% and 1.0%, respectively. The extractive value was 84% w/w. Tea Tree Oil was obtained as a clear, colourless liquid with a characteristic odour. Its specific gravity was found to be 0.8868 and the λmax was 267 nm. These preformulation findings provided useful information for the subsequent formulation studies.

The niosomal formulations F1–F4 were prepared using different concentrations of Span 20 and stearic acid while maintaining the quantities of Curcumin and Tea Tree Oil constant. The variation in the formulation composition produced differences in the physicochemical characteristics of the prepared niosomes. Among the formulations, F3 showed the most satisfactory overall characteristics and was therefore selected as the optimized niosomal formulation.

The optimized F3 formulation exhibited a particle size of 286 nm with a PDI of 0.287. The nanosized particle size indicates the formation of a vesicular system suitable for investigation as a topical nanocarrier, while the PDI value indicates a relatively uniform particle-size distribution. The zeta potential of F3 was found to be −32.4 mV. The presence of surface charge may contribute to repulsion between vesicles and thereby support the physical stability of the niosomal dispersion.

F3 showed an entrapment efficiency of 84.7%, indicating effective incorporation of Curcumin into the niosomal vesicles. The drug content of F3 was 97.1%, demonstrating satisfactory drug incorporation within the optimized formulation. Considering the particle size, zeta potential, entrapment efficiency and drug content, F3 was selected for incorporation into the gel base.

The optimized niosomal dispersion was incorporated into a Carbopol 934 gel base enriched with Aloe vera to obtain the niosomal gel formulations G1–G3. The prepared gel formulations showed smooth and uniform characteristics without visible phase separation. The pH values of the formulations were within an acceptable range for topical application, indicating their suitability for further evaluation.

Among the prepared gel formulations, G3 exhibited the highest viscosity of 10308 cP. The viscosity indicates that the formulation possessed adequate consistency for topical application. The spreadability results demonstrated that the optimized gel could spread over the surface when an external weight was applied, which is important for convenient application over the affected skin area. The extrudability values of G1, G2 and G3 were 0.080, 0.085 and 0.090 g/sec, respectively, indicating that the formulations could be readily removed from their container.

The drug content of the prepared gel formulations was found to be 94.26%, 96.18% and 98.42% for G1, G2 and G3, respectively. G3 showed the highest drug content among the prepared formulations. Based on its overall appearance, homogeneity, pH, viscosity, spreadability, extrudability and drug content, G3 was selected as the optimized niosomal gel formulation.

Overall, the results demonstrate the feasibility of incorporating Curcumin and Tea Tree Oil into a niosomal system and subsequently incorporating the optimized niosomes into an Aloe vera-enriched Carbopol 934 gel. The optimized formulation showed satisfactory physicochemical characteristics and therefore represents a potential polyherbal topical delivery system for acne management. Further studies such as in-vitro drug release, skin permeation, antimicrobial activity and stability studies are required to establish its performance and therapeutic potential.

CONCLUSION

The present study was successfully carried out through preformulation studies and systematic evaluation of the prepared niosomal formulations and niosomal gel, leading to the following conclusions:

The preformulation studies of Curcumin, including authentication, organoleptic properties, solubility, melting point, moisture content, UV spectrophotometric analysis, ash value, extractive value, and preliminary phytochemical screening, were performed and the obtained results were found to be satisfactory for further formulation development. The preformulation studies of Tea Tree Oil, including authentication, organoleptic properties, solubility study, specific gravity, UV spectrophotometric analysis, partition coefficient, and preliminary phytochemical screening, were carried out and the results supported its suitability for incorporation into the formulation.

The prepared niosomal formulations were evaluated for appearance, homogeneity, pH, particle size, zeta potential, entrapment efficiency, and drug content. Among the prepared formulations, F3 was selected as the optimized niosomal formulation based on its satisfactory evaluation characteristics.

The optimized F3 niosomal formulation was incorporated into a Carbopol 934 gel base enriched with Aloe vera to develop a topical niosomal gel.

The prepared niosomal gel formulations were evaluated for appearance, homogeneity, pH, viscosity, spreadability, extrudability, and drug content. Among the prepared gel formulations, G3 was selected as the optimized niosomal gel formulation based on its satisfactory physicochemical characteristics.

The optimized G3 niosomal gel exhibited suitable physicochemical properties, including acceptable appearance and homogeneity, skin-compatible pH, suitable viscosity, good spreadability and extrudability, and satisfactory drug content, indicating its potential suitability for topical application.

Hence, the study successfully demonstrated the feasibility of developing a Curcumin and Tea Tree Oil-loaded niosomal gel enriched with Aloe vera as a potential polyherbal topical formulation for the management of acne.

ACKNOWLEDGEMENT

The authors sincerely express their gratitude to Mrs. Anju K. P., Department of Pharmaceutics, Spurthy College of Pharmacy, Bengaluru, for her valuable guidance, continuous support, and encouragement throughout this research work. The authors also thank the management, Principal, faculty members, and staff of the institution for providing the necessary facilities and support for the successful completion of this study.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

1. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. Lancet. 2012;379(9813):361-72.
2. Reynolds RV, Yeung H, Cheng CE, Cook-Bolden F, Desai SR, Druby KM, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2024;90(5):1006.e1-1006.e30.
3. Nast A, Dréno B, Bettoli V, Bukvic Mokos Z, Degitz K, Dressler C, et al. Adverse events related to topical drug treatments for acne vulgaris. J Eur Acad Dermatol Venereol. 2020;34(5):1035-44.
4. Walsh TR, Efthimiou J, Dréno B. Systematic review of antibiotic resistance in acne: an increasing topical and oral threat. Lancet Infect Dis. 2016;16(3):e23-33.
5. Vaughn AR, Branum A, Sivamani RK. Effects of turmeric (Curcuma longa) on skin health: a systematic review of the clinical evidence. Phytother Res. 2016;30(8):1243-64.
6. Moballegh Nasery M, Abadi B, Poormoghadam D, Zarrabi A, Keyvani V, Khanbabaei H, et al. Emerging trends in topical delivery of curcumin through lipid nanocarriers: effectiveness in skin disorders. AAPS PharmSciTech. 2020;21(8):348.
7. Carson CF, Hammer KA, Riley TV. Melaleuca alternifolia (tea tree) oil: a review of antimicrobial and other medicinal properties. Clin Microbiol Rev. 2006;19(1):50-62.
8. Enshaieh S, Jooya A, Siadat AH, Iraji F. The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study. Indian J Dermatol Venereol Leprol. 2007;73(1):22-25.
9. Feily A, Namazi MR. Aloe vera in dermatology: a brief review. G Ital Dermatol Venereol. 2009;144(1):85-91.
10. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. J Pharm Pharmacol. 1998;50(6):617-28.
11. Manosroi A, Wongtrakul P, Manosroi J, Sakai H, Sugawara F, Yuasa M, et al. Characterization of niosomes prepared from novel nonionic surfactants: synthesis, toxicity and drug release study. J Pharm Pharm Sci. 2003;6(3):390-400.
12. Goyal G, Garg T, Malik B, Chauhan G, Rath G, Goyal AK. Development and characterization of niosomal gel for topical delivery of benzoyl peroxide. Drug Deliv. 2015;22(8):1027-42.
13. Akbarzadeh A, Sabouri Z, Khosroushahi AY, Tazikeh-Laridjani B, Rezaei-Sadabadi M, Hashemi M, et al. Solubility enhancement and delivery systems of curcumin a herbal medicine: a review. Curr Pharm Des. 2014;20(32):5104-14.
14. Pazyar N, Yaghoobi R, Bagherani N, Kazerouni A. A review of applications of tea tree oil in dermatology. Int J Dermatol. 2013;52(7):784-90.
15. Thabet Y, Elsabahy M, Eissa NG. Methods for preparation of niosomes: a focus on thin-

film hydration method. Methods. 2022;199:9-15.
16. Gawade S, Attimarad S, Desai V. A systematic review on niosomes: composition, preparation, and applications. Manipal J Med Sci. 2026;10(1):Article 3.
17. Mawazi SM, Ge Y, Widodo RT. Niosome preparation techniques and structure—an illustrated review. Pharmaceutics. 2025;17(1):67.
18. Kaur D, Garg T, Rath G, Goyal AK. Surfactant-based drug delivery systems: a review. Drug Dev Ind Pharm. 2014;40(11):1395-1406.
19. Amreen A, KV R. Formulation and evaluation of tramadol hydrochloride-loaded niosomal gel by ether injection method. Asian J Pharm Clin Res. 2023;16:170-3.
20. Bassett IB, Pannowitz DL, Barnetson RS. A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. Med J Aust. 1990;153(8):455-8.
21. Balakrishnan P, Shanmugam S, Lee WS, Lee WM, Kim JO, Oh DH, et al. Formulation and in vitro assessment of minoxidil niosomes for enhanced skin delivery. Int J Pharm. 2009;377(1-2):1-8.
22. Das MK, Palei NN. Sorbitan ester niosomes for topical delivery of rofecoxib. Indian J Exp Biol. 2011;49(6):438-45.
23. Okore VC, Attama AA, Ofokansi KC, Esimone CO, Onuigbo EB. Formulation and evaluation of niosomes. Indian J Pharm Sci. 2011;73(3):323-8.
24. Varshosaz J, Pardakhty A, Hajhashemi V, Rouholamini Najafabadi A. Development and physical characterization of sorbitan monoester niosomes for insulin oral delivery. Drug Deliv. 2003;10(4):251-62.
25. Sezgin Z, Yuksel N, Bayindir ZS. Characterization of niosomes prepared with various nonionic surfactants for paclitaxel oral delivery. J Pharm Sci. 2010;99(4):2049-60.
26. Ravouru N, Kondreddy P, Korakanchi D, Haritha M. Formulation and evaluation of niosomal nasal drug delivery system of folic acid for brain targeting. Curr Drug Discov Technol. 2013;10(4):270-82.
27. Sguizzato M, Pepe A, Baldisserotto A, Barbari R, Montesi L, Drechsler M, et al. Niosomes for topical application of antioxidant molecules: design and in vitro behavior. Gels. 2023;9(2):107.
28. Shehata TM, Ibrahim MM, Elsewedy HS. Curcumin niosomes prepared from proniosomal gels: in vitro skin permeability, kinetic and in vivo studies. Polymers (Basel). 2021;13(5):791.
29. Akbari J, Saeedi M, Morteza-Semnani K, Hashemi SMH, Babaei A, Rahimnia SM, et al. Innovative topical niosomal gel formulation containing diclofenac sodium (niofenac). J Drug Target. 2022;30(1):108-17.
30. Manconi M, Sinico C, Valenti D, Loy G, Fadda AM. Niosomes as carriers for tretinoin. I. Preparation and properties. Int J Pharm. 2002;234(1-2):237-48.
31. Manconi M, Valenti D, Sinico C, Lai F, Loy G, Fadda AM. Niosomes as carriers for tretinoin. II. Influence of vesicular incorporation on tretinoin photostability. Int J Pharm. 2003;260(2):261-72.
32. Manconi M, Sinico C, Valenti D, Lai F, Fadda AM. Niosomes as carriers for tretinoin. III. A study into the in vitro cutaneous delivery of vesicle-incorporated tretinoin. Int J Pharm. 2006;311(1-2):11-9.
33. Mali N, Darandale S, Vavia P. Niosomes as a vesicular carrier for topical administration of minoxidil: formulation and in vitro assessment. Drug Deliv Transl Res. 2013;3(6):587-92.

34. Manca ML, Manconi M, Nacher A, Carbone C, Valenti D, Maccioni AM, et al. Development of novel diolein-niosomes for cutaneous delivery of tretinoin: influence of formulation and in vitro assessment. Int J Pharm. 2014;477(1-2):176-86.
35. Kaur K, Jain S, Sapra B, Tiwary AK. Niosomal gel for site-specific sustained delivery of anti-arthritic drug: in vitro-in vivo evaluation. Curr Drug Deliv. 2007;4(4):276-82.
36. Eshun K, He Q. Aloe vera: a valuable ingredient for the food, pharmaceutical and cosmetic industries—a review. Crit Rev Food Sci Nutr. 2004;44(2):91-6.
37. Hamman JH. Composition and applications of Aloe vera leaf gel. Molecules. 2008;13(8):1599-1616.
38. Surjushe A, Vasani R, Saple DG. Aloe vera: a short review. Indian J Dermatol. 2008;53(4):163-6.
39. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The effect of Aloe vera clinical trials on prevention and healing of skin wound: a systematic review. Iran J Med Sci. 2019;44(1):1-9.
40. Liang J, Cui L, Li J, Guan S, Zhang K, Li J. Aloe vera: a medicinal plant used in skin wound healing. Tissue Eng Part B Rev. 2021;27(5):455-74.
41. Paulsen E, Korsholm L, Brandrup F. A double-blind, placebo-controlled study of a commercial Aloe vera gel in the treatment of slight to moderate psoriasis vulgaris. J Eur Acad Dermatol Venereol. 2005;19(3):326-31.
42. Syed TA, Ahmad SA, Holt AH, Ahmad SA, Ahmad SH, Afzal M. Management of psoriasis with Aloe vera extract in a hydrophilic cream: a placebo-controlled, double-blind study. Trop Med Int Health. 1996;1(4):505-9.
43. Chithra P, Sajithlal GB, Chandrakasan G. Influence of Aloe vera on collagen characteristics in healing dermal wounds in rats. Mol Cell Biochem. 1998;181(1-2):71-76.
44. Heggers JP, Kucukcelebi A, Listengarten D, Stabenau J, Ko F, Broemeling LD, et al. Beneficial effect of Aloe on wound healing in an excisional wound model. J Altern Complement Med. 1996;2(2):271-7.
45. Boudreau MD, Beland FA. An evaluation of the biological and toxicological properties of Aloe barbadensis (Miller), Aloe vera. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2006;24(1):103-54.
46. Trottet L, Merly C, Mirza M, Hadgraft J, Davis AF. Effect of finite doses of propylene glycol on enhancement of in vitro percutaneous permeation of loperamide hydrochloride. Int J Pharm. 2004;274(1-2):213-19.
47. Yu HL, Goh CF. Glycols: the ubiquitous solvent for dermal formulations. Eur J Pharm Biopharm. 2024;196:114182.
48. Fluhr JW, Darlenski R, Surber C. Glycerol and the skin: holistic approach to its origin and functions. Br J Dermatol. 2008;159(1):23-34.
49. Verdier-Sévrain S, Bonté F. Skin hydration: a review on its molecular mechanisms. J Cosmet Dermatol. 2007;6(2):75-82.
50. Mura S, Pirot F, Manconi M, Falson F, Fadda AM. Liposomes and niosomes as potential carriers for dermal delivery of minoxidil. J Drug Target. 2007;15(2):101-8.

HOW TO CITE: Swetha V, Navyashree V, Chandana V, Amaldev K M, Abin T S, Anju K P, Curcumin and Tea Tree Oil-Loaded Niosomal Gel with Aloe Vera: A Polyherbal Approach to Anti-Acne Therapy, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 9, 2315-2346, https://doi.org/10.5281/zenodo.22867615