RESEARCH PAPER

Formulation, Evaluation and Comparative Study of Topical Dosage Form of Curcumin and Alpha Tocopherol Loaded NLC's

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ABSTRACT

Curcumin and α-tocopherol are well-known natural antioxidants possessing antioxidant, anti-inflammatory, antimicrobial, and wound-healing properties. However, their therapeutic application is limited by poor aqueous solubility, low stability, rapid degradation, and inadequate skin penetration. The present study was undertaken to formulate Curcumin–α-Tocopherol-loaded Nanostructured Lipid Carriers (NLCs) and to comparatively evaluate their incorporation into topical gel and cream formulations for enhanced dermal drug delivery. The NLCs were prepared using a lipid matrix comprising Compritol® 888 ATO, α-tocopherol, Tween 80, and Poloxamer 188 through ultrasonication, followed by optimization and physicochemical characterization. The optimized NLCs were evaluated for particle size, polydispersity index, zeta potential, morphology, FTIR compatibility, encapsulation efficiency, drug loading, in vitro drug release, antibacterial activity, and stability. The optimized NLCs were subsequently incorporated into Carbopol 940 gel and oil-in-water cream bases and evaluated for appearance, homogeneity, pH, viscosity, spreadability, drug content, in vitro diffusion, stability, and antimicrobial activity. The gel formulation demonstrated better spreadability and faster drug diffusion, whereas the cream exhibited higher viscosity and a more sustained drug release profile. Both formulations remained physically stable throughout the storage period and showed significant antibacterial activity against Escherichia coli and Staphylococcus aureus, with the NLC-loaded gel producing comparatively larger zones of inhibition than the cream formulation. The comparative evaluation indicated that both dosage forms effectively delivered Curcumin and α-tocopherol; however, the gel provided superior antimicrobial efficacy and drug diffusion, while the cream offered prolonged retention and sustained release. These findings suggest that Curcumin–α-Tocopherol-loaded NLCs represent a promising lipid-based platform for topical therapy and that formulation selection can be tailored according to the desired therapeutic outcome.

Keywords: Curcumin; α-Tocopherol; Nanostructured Lipid Carriers (NLCs); Topical Gel; Topical Cream; Comparative Evaluation.

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Conflict of interest: None

1. INTRODUCTION

Nanotechnology is one of the most promising approaches in pharmaceutical sciences with applications in medicine, cosmetics, environmental science and nutraceuticals. Nanocarrier based drug delivery systems have attracted much attention due to enhancement of therapeutic performance of drugs by solubility, stability, bioavailability, controlled release and site-specific targeting. Nanoparticles exhibit unique physicochemical properties, like a high surface-area-to-volume ratio and nanoscale size, which allow them to interact effectively with biological membranes and possess better pharmacokinetics than conventional dosage forms. In addition, nanocarriers can be designed to reduce toxicity and increase therapeutic efficacy by modifying their composition, surface properties and morphology [1].

Over the last few years, antioxidant compounds have been the subject of researchers' interest due to their diverse dermatological, pharmaceutical, and biological functions. These compounds have free radical scavenging, melanin reduction, wound healing and light protection properties [2,3]. Curcumin (cur) is a lipophilic polyphenol isolated from the rhizome of Curcuma longa [4]. The cur has been demonstrated to possess biological activities including antioxidant, anti-inflammatory, antimicrobial, anticancer and wound-healing effects [5]. On the other hand, α-tocopherol (α -toc) is the most active and effective form of vitamin E, widely distributed in nature, and used as an antioxidant in the food, cosmetics

and pharmaceutical industries [6–8]. Moreover, topical application of α-toc has been demonstrated to safeguard the skin and accelerate wound healing [9]. Furthermore, α-toc due to its peroxyl radical scavenging activity can help to protect the phospholipids and fatty acids in the membrane of the skin [2]. The therapeutic value of cur and α-toc in dermatology is remarkable, but is limited by several factors. Cur has poor aqueous solubility (< 0.1 mg/mL), low physicochemical stability, unsustainable bioavailability, low skin permeability and fast metabolism, consequently, low cur levels in tissues [10–13]. On the other hand, α-toc is easily oxidized by atmospheric oxygen, has low solubility in water (~30 mg/L) and high sensitivity to light, and some skin irritation issues have been described limiting its application and incorporation in products [14,15]. These challenges are major obstacles to the best topical and systemic efficacy of cur and α-toc. The development of co-encapsulation delivery systems to overcome these drawbacks has several advantages including protection of therapeutic molecules and integrity, facilitation of incorporation, formulation flexibility in terms of ratio and dosage, controlled release capabilities and the potential for synergistic effects when multiple therapeutic molecules are incorporated [16,17].The development of new co-encapsulation administration systems is important for the development of new products for dermatological applications [18].

Curcumin is a naturally occurring polyphenolic compound, isolated from rhizomes of Curcuma longa having several pharmacological activities like antioxidant, anti-inflammatory, antimicrobial, anticancer and wound healing. Curcumin has therapeutic potential but its clinical application is limited due to very low aqueous solubility, poor gastrointestinal absorption, rapid metabolism, chemical instability and low bioavailability. Thus, many formulation strategies have been explored to overcome these limitations and improve its therapeutic efficacy [19].

α-Tocopherol (Vitamin E) is an important lipid soluble antioxidant and the most active form of vitamin E in biological systems. It scavenges lipid peroxyl radicals and inhibits lipid peroxidation, thereby protecting biological membranes from oxidative damage. α-Tocopherol has been widely used in pharmaceutical and cosmetic formulations owing to its antioxidant, anti-inflammatory, photoprotective and wound-healing properties. However, its therapeutic application is restricted by poor aqueous solubility, sensitivity to light and oxygen, oxidative degradation during storage and limited skin penetration. Hence, it is less stable and has reduced clinical efficacy [1].

Co-delivery of curcumin and α-tocopherol is an attractive therapeutic approach as both compounds have complementary antioxidant and anti-inflammatory mechanisms. The co-delivery of these bioactive molecules can provide synergistic protection against oxidative stress, as well as enhanced wound healing, antimicrobial activity and skin regeneration. However, co-delivery of two compounds needs an appropriate carrier system to protect both compounds from degradation, maintain controlled release, and improve skin penetration [1].

Nanostructured lipid carriers (NLCs) are the second generation of lipid nanoparticles and have been developed to overcome the limitations of conventional solid lipid nanoparticles (SLNs). NLCs are made from a mixture of solid and liquid lipids which results in an imperfect crystalline matrix with higher capacity to accommodate drug. The novel lipid architecture shows better encapsulation efficiency, lesser drug leakage during storage, better physicochemical stability and sustained drug release. Furthermore, owing to their nanoscale size, they are able to interact closely with the stratum corneum, thus improving skin permeation and drug retention in epidermal and dermal tissues. These properties make NLCs very good carriers for lipophilic bioactives like curcumin or α-tocopherol [1].

The encapsulation of curcumin in lipid-based Nano formulations has been demonstrated to considerably enhance its stability, solubility, bioavailability, antioxidant activity and therapeutic efficacy (Omer et al., 2018; Tsai et al., 2018). α-tocopherol loaded lipid nanoparticles have been reported to show similar improvements in oxidation protection and increased biological activity (Yin et al., 2018). Recent studies also indicate that the co-encapsulation of different antioxidants into a single lipid nanocarrier provides greater stability and a better antioxidant effect than single delivery systems, as the encapsulated compounds have complementary protective mechanisms [1].

In this present study, co-encapsulation of Curcumin and α-Tocopherol into Nanostructured Lipid Carriers (Cur/α-Toc-NLCs) was carried out for improving their physicochemical stability, encapsulation efficiency, controlled release properties and topical delivery. The formulation of NLCs were characterized for particle size, polydispersity index (PDI), zeta potential, morphology, Fourier Transform Infrared Spectroscopy (FTIR), encapsulation efficiency, drug loading, in vitro drug release, antioxidant activity, antibacterial activity and stability.

The optimized Cur/α-Toc loaded NLCs are separately loaded into topical gel and cream formulations for development of patient friendly dosage forms for dermal application. The physicochemical parameters such as pH, viscosity, spreadability, drug content, extrudability, homogeneity, in vitro diffusion, skin permeation and

stability and antimicrobial activity of both the topical formulations were evaluated. Finally, comparative evaluation is carried out between NLC loaded gel and NLC loaded cream to find out the best topical delivery system based on drug release behavior, skin retention, stability and therapeutic efficacy. This holistic approach is applied for the development of a robust lipid-based topical drug delivery platform that will increase the therapeutic benefits of curcumin and α-tocopherol for dermatological applications [1].

2. MATERIALSANDMETHODS

2.1 Materials

The α-Tocopherol was procured from authentic sources which include Merk Limited India and the *Curcuma longa* (turmeric) plant was collected from its natural habitat in Sirmaur District of Himachal Pradesh, India. The drug and excipient constituents used for the preparation of Nano lipid carrier system and topical drug delivery system of different formulations were prepared and evaluated. The formulations were prepared using analytical grade compounds without further purification.

2.2. Formulation of Topical Drug Delivery System

2.2.1 Formulation of Cream

The cream formulation was prepared by separately preparing the oil and aqueous phases. The oil phase ingredients were accurately weighed and heated to 70°C with continuous stirring using a mechanical stirrer at 100 rpm until a uniform liquid was obtained. Similarly, the aqueous phase ingredients were weighed, heated to 70°C, and stirred at 100 rpm to obtain a homogeneous solution. The heated oil phase was then gradually added to the aqueous phase while maintaining the temperature at 70°C, followed by continuous stirring at 1000 rpm for 30 minutes to form a uniform cream base. Subsequently, different concentrations of Curcumin-loaded Nanostructured Lipid Carriers (Cur-NLCs) and α-Tocopherol were incorporated into the prepared cream base under continuous stirring at 1000 rpm until a homogeneous dispersion was achieved. The prepared formulations were allowed to equilibrate at room temperature for 24 hours, after which the creams were filled into wide-mouth polypropylene containers and stored for further physicochemical and pharmaceutical evaluation [20].

2.2.2 Composition of Cream formulations

Table .1. Composition of Cream Base

Ingredients	Formulations codes (w/w)				
	FC1	FC2	FC3	FC4	FC5
Stearic acid	3%	3%	2.5%	2.5%	2.0%
Castor oil	15%	15%	15%	15%	15%
Bees wax	7%	7%	7%	7%	7%
Cetyl alcohol	2%	2%	2%	2%	2%
Paraffin wax	2%	1.5%	1.5%	2%	2.%
Triethanolamine	1.78%	1.78.%	1.78%	1.78%	1.78%
Glycerine	5%	5%	5%	5%	5%
water	To 100	To 100	To 100	To 100	To 100
Fragrance	q.s	q.s	q.s	q.s	q.s

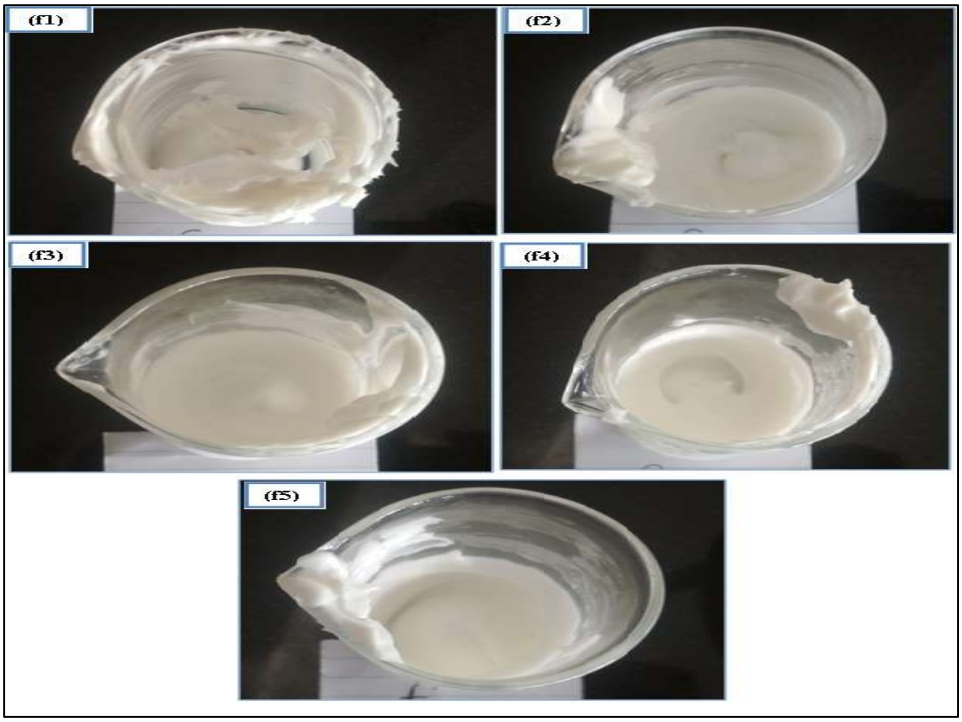

Figure.1. Image showing different cream base formulations

2.2.3 Incorporation of CNL into Cream Base

Curcumin-loaded NLCs (CNL) were then incorporated into the cream base under continuous overhead stirring at 800 rpm using a Remi stirrer (Mumbai, India) until a uniform dispersion was achieved. The dispersion was neutralized using triethanolamine to adjust the pH, resulting in the formation of a stable cream.[21]

Table.2. Composition of Cream Base (F3) with drug

Ingredients	Formulations codes (w/w)			
	FC3	FC3 + α-Tocopherol	FC3 + Curcumin	FC3 + α-Tocopherol + Curcumin NLC
α-Tocopherol	-	2%	-	2%
Curcumin NLC	-	-	10%	10%
Stearic acid	2.5%	2.5%	2.5%	2.5%
Castor oil	15%	15%	15%	15%
Bees wax	7%	7%	7%	7%
Cetyl alcohol	2%	2%	2%	2%
Paraffin wax	1.5%	1.5%	1.5%	1.5%
triethanolamine	1.78%	1.78.%	1.78%	1.78%
glycerine	5%	5%	5%	5%
water	To 100	To 100	To 100	To 100
fragrance	q.s	q.s	q.s	q.s

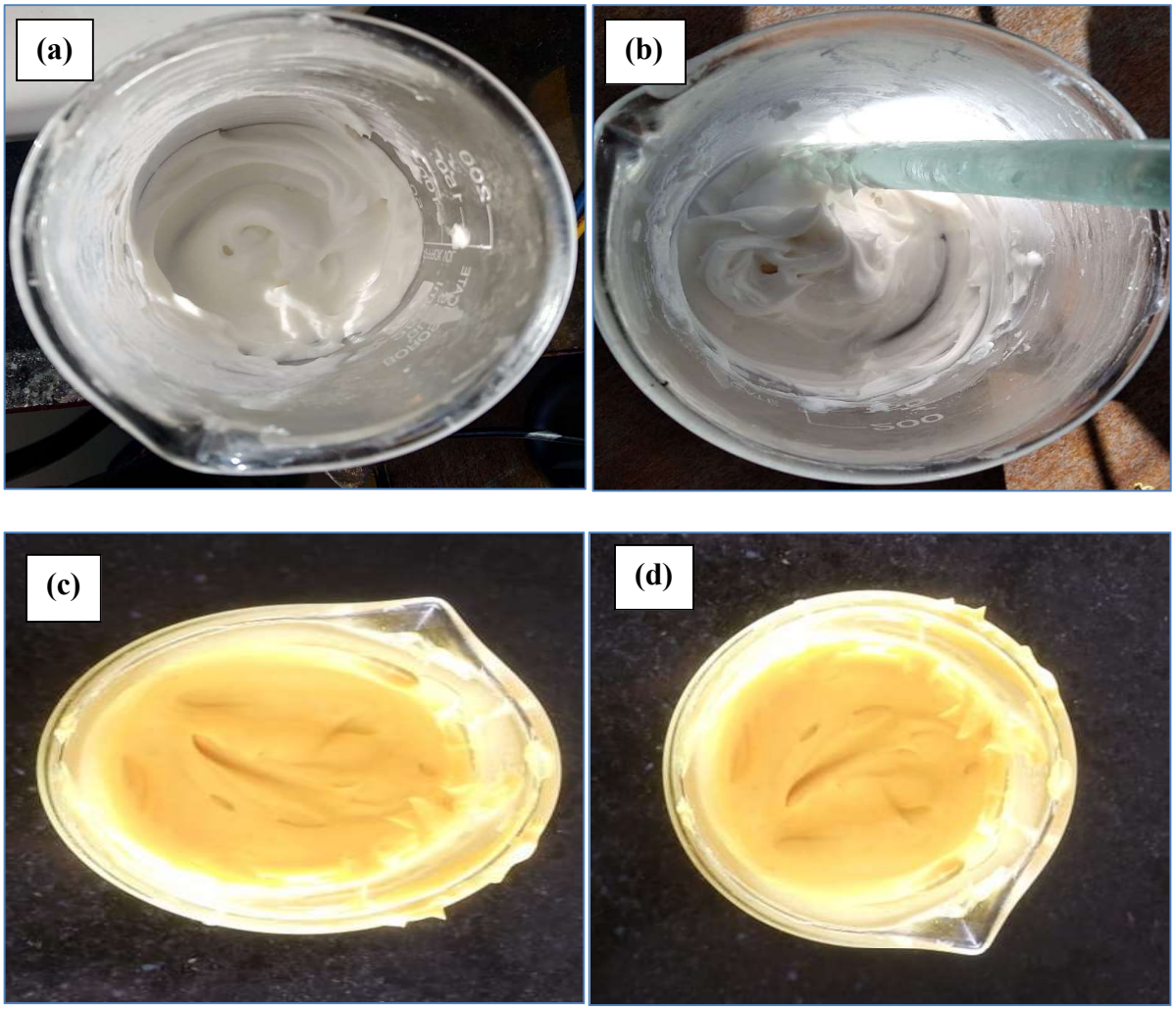

Figure.2. Image showing blank cream base (a), α-tocopherol incorporated cream (b), Curcumin NLC loaded cream (c) and cream with α-tocopherol &Curcumin NLC (d) respectively.

2.3 Formulation of gel

2.3.1 Preparation of gelling base

Carbopol 940 was dispersed in distilled water at varying concentrations (0.25%, 0.5,1%, 1.5% and 2.0% w/v) and allowed to hydrate overnight. The concentration that yielded a stable and homogenous gel was selected as the gelling base for the formulation of the curcumin-loaded NLC (CNL)-based gel [20].

2.3.2 Different formulation of gelling base

Table.3. Compositions of gelling base

Ingredients	Formulations codes (w/w)				
	FG1	FG2	FG3	FG4	FG5
Carbopol 940	0.25%	0.5%	1.0%	1.5%	2.0%
HPMC	0.5%	0.5%	0.5%	0.5%	0.5%
Triethanolamine	1%	1%	1%	1%	1%
glycerin	5%	5%	5%	5%	5%
Distilled water (ml)	QS	QS	QS	QS	QS

Figure.3. Representing Gel base formulation

2.3.3 Incorporation of CNL into Gel Base

Curcumin-loaded NLCs (CNL) were then incorporated into the Carbopol 940 gel base under continuous overhead stirring at 800 rpm using a Remi stirrer (Mumbai, India) until a uniform dispersion was achieved. The dispersion was neutralized using triethanolamine to adjust the pH, resulting in the formation of a stable gel.[21]

Table.4. Composition of Gel Base (F2) with drug

Ingredients	Formulations codes (w/w)			
	FG2	FG2+ α-Tocopherol	FG2 + Curcumin	FG2 + α-Tocopherol + Curcumin NLC
α-Tocopherol	-	2%	-	2%
Curcumin NLC	-	-	10%	10%
Carbopol 940	0.25%	0.5%	1.0%	1.5%
HPMC	0.5%	0.5%	0.5%	0.5%
Triethanolamine	1%	1%	1%	1%
glycerine	5%	5%	5%	5%
Distilled water (ml)	QS	QS	QS	QS

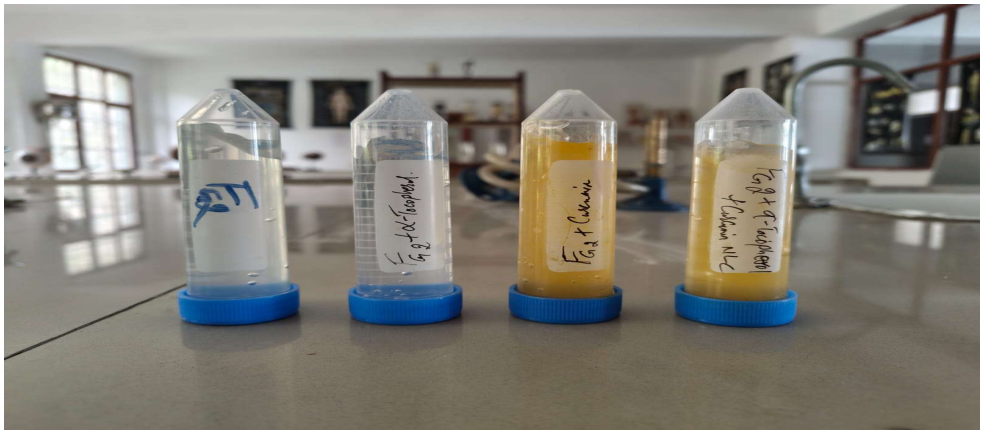

Figure.4. Representing α-Tocopherol + Curcumin NLC loaded Gel

3. EVALUATION PARAMETERS OF TOPICAL FORMULATIONS

3.1 Physical parameters

3.1.1 Appearance

All the formulated creams were tested for the color diversity by visual inspection. They were checked against white background.

3.1.2 Odor

The odor of all formulated creams was analysed.

3.1.3 Consistency

The consistency of the formulated cream/gel was evaluated by visual inspection and manual examination using a glass rod or spatula to assess its uniformity, texture and ease of spreading.

3.1.4 Greasiness

The greasiness of the formulation was evaluated by visual examination and by rubbing a small quantity between two glass rods (or gloved finger) to assess the oily residue.

3.1.5 Homogeneity

All developed creams were tested for homogeneity by visual inspection. They were checked for their appearance and presence of any aggregates [22].

3.2 Pharmaceutical Parameters

3.2.1 pH determination

The pH of formulated creams was initially determined by using pH strip. After satisfactory outcomes from the pH strip, prepared cream was further subjected to digital pH meter for in depth clarification of pH. 1% solution of the formulation was prepared using distilled water. The pH of each formulation was monitored in triplicate and average values were calculated. [23]

3.2.2 Viscosity Study

The viscosity determinations were carried out using a Brookfield Viscometer (DVE model) using spindle number S64 at a 1.0 rpm at a temperature of 25oC. The determinations were carried out in triplicate, the average of three readings was recorded.[24]

Figure.5. Representing Brookfield viscometer determining viscosity of formulation.

3.2.3 Spreadability

Spreadability may be expressed by the extent of the area to which the topical application spreads when applied to the affected parts on the skin. The therapeutic efficiency of the formulation also depends upon its spreading value. Hence, it was found necessary to determine the spread ability of the formulation. For this purpose, sample (about 1gm) was applied in between two glass slides and they were pressed together to obtain a film of uniform thickness by placing 10gm weight for 5 minutes. Thereafter a weight (50gm) was added to the pan and the top plate was subjected to pull with the help of string attached to the hook. The time in which the upper glass slide moves over the lower plate to cover a distance of 10 cm is noted. The spread ability (S) can be calculated using the formula. [25]

$$S = M \times L / T \qquad \text{Eq……. (1)}$$

Where,

S– Spread ability- Weight tied to upper glass slide, ***L***- Length moved on a glass slide and ***T***- Time taken. The determinations were carried out in triplicate and the average of three readings was recorded.

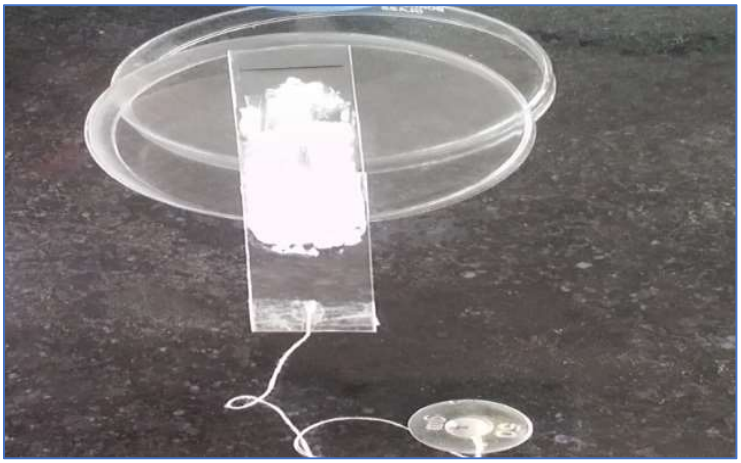

Figure.6. Image representing the investigation of Spreadability for distinct creams

3.2.4 In-Vitro Drug release Studies

Because the egg membrane and the stratum corneum of human skin are similar, the permeation investigation was conducted utilizing the egg membrane. Fresh eggs were procured from local retail shops, which were then stored for two hours in a diluted hydrochloric acid solution (0.1 N). The membrane had been removed once the eggshell was disintegrated. After being cleaned with deionized water, the membrane was allowed to air dry at room temperature and used as a biological membrane for in vitro drug release studies.

The eggshell membrane was secured tightly with thread after a weighed amount of NLC dispersion and an equivalent quantity of NLC gel (depending on drug content) were each placed within. To guarantee proper solubility and sink conditions, the sealed membrane sacs were submerged in 400 mL of a receptor medium made up of a 70:30 (v/v) mixture of ethanol and phosphate buffer saline (PBS, pH 5.5). In order to replicate the skin surface temperature, the setup was kept at a steady 32 ± 0.5 °C. A 500–750 rpm stirrer was used to provide constant stirring. To maintain the volume and sink conditions, 1 mL portions of the receptor medium were taken out and promptly replenished with an equivalent volume of new medium at specific periods of time. Using UV-visible spectrophotometry at the drug's specific λmax, the drug content of the withdrawn samples was examined in order to calculate the cumulative drug release over time.[26]

Finally, a Graph was plotted between % cumulative drug release (CDR) v/s time and release profile of formulation was compared with each other.

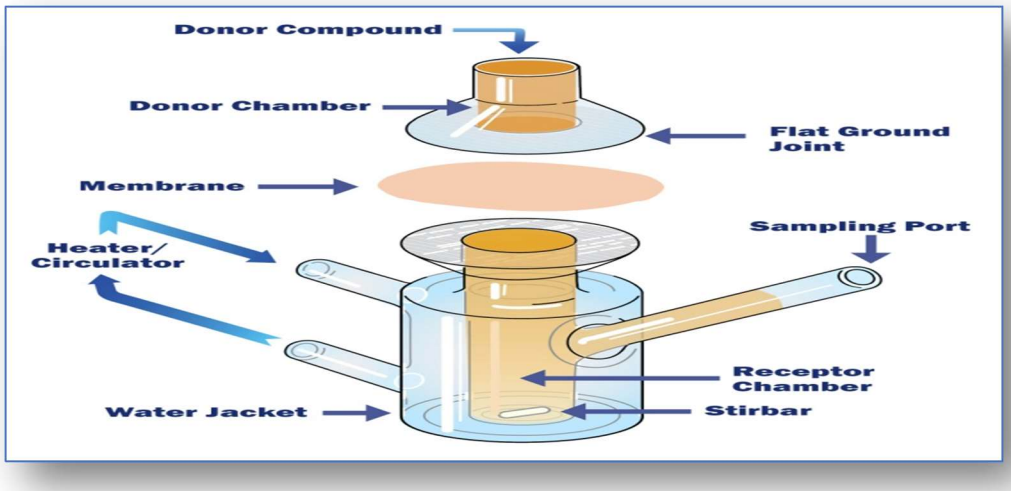

Figure.7. Image Showing the Different Compartment of Franz Diffusion cell (Image acquired from the review paper of AshishAswal et al.).

3.2.5 Stability study

Stability studies of cream were performed according to the international conference on Harmonization (ICH) harmonized guidelines on stability testing of new drug substance and product. The optimized cream and Gel formulation (FC3 + α-Tocopherol + Curcumin NLC and FG2 + α-Tocopherol + Curcumin NLC) was tested for stability under two conditions for a period of two months. The cream was kept in sterile lacquered collapsible aluminum tubes and stored in stability chamber maintained at 4oC and room temperature. Formulation was evaluated for their physical characteristics, pH, and content of active ingredient at the end of 1 day, 15 days, 30 days, 45 days and 60 days of storage period.[27]

3.2.6 Antibacterial Assay

The antibacterial efficacy of drug loaded NLCs against Escherichia coli and Streptococcus aureus was studied by using liquid and solid media methods [28,29]

3.2.6.1 Quantitative Antibacterial Analysis in Liquid Medium

Activated bacterial cultures were incubated with various formulations of NLC mixed with LB broth medium. The cultures were shaken periodically and maintained at 37°C. The percent of bacterial inhibition was calculated using the following formula [29].

Bacterial Inhibition (%) =Ic−Is / Ic ×100

3.2.6.2 Qualitative Antibacterial Assessment in Solid Medium

Antibacterial activity was also estimated by agar well diffusion method. We cut wells in the LB agar plates with a sterile borer and spread the bacterial suspension evenly on the plates. The formulations were filled in the wells and the plates were kept at 37 °C for a complete day. The inhibition zone was assessed and compared to other formulations [29]

4. RESULTS AND DISCUSSION

4.1.1 Preformulation studies of drugs

Pre-formulation studies of curcumin were conducted and compared with standard. It was observed that the melting point of the sample was almost same as that of the standard. Sample and standard were similar. The solubility of the different samples of medication was also found to be the same as the standard. No change in the wavelengths of the associated samples was observed with respect to individual standards.

Table.5. Preformulation studies of Curcumin

Sr. No.	Parameters	Standard	Sample
1	Melting Point	183^0C	180^0C
2	Appearance	Yellowish-orange powder	Yellowish-orange powder
3	Solubility	Ethanol	Ethanol
4	Wavelength	420nm	423nm

4.1.2 Solubility studies

It was clear from the solubility studies that Curcumin showed high solubility in Ethanol in contrast to other solvents

Table.6. Solubility study of drug in different solvents

Sr. No	Solvents used	Curcumin
1	Water	++
2	Methanol	++
3	Buffer	+
4	Ethanol (95%)	+++

Highly soluble +++, Soluble ++, poorly soluble +

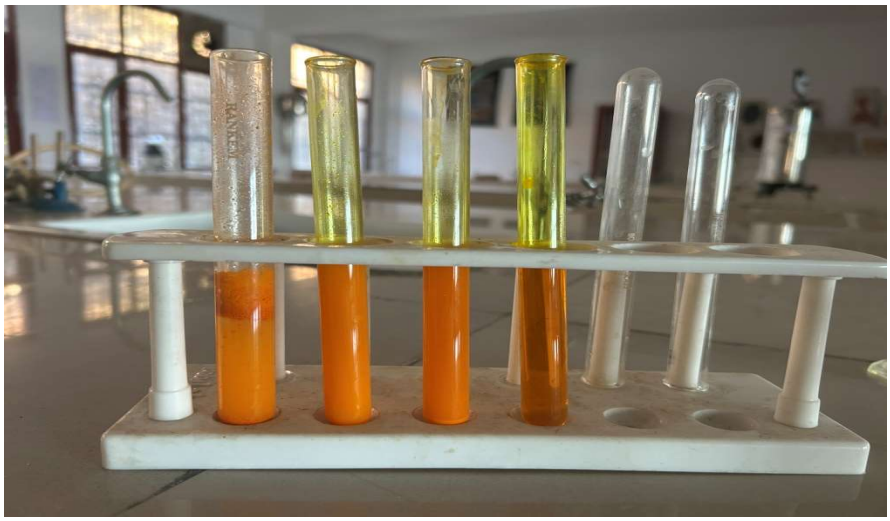

Figure.8. Image representing the investigation of Solubility

4.1.3 Preformulation studies of drugs

The pre-formulation studies of Alpha Tocopherol were carried out and compared with standards. It was observed that the melting point of the sample was approximately equal to that of the standard. The appearances of the standard and the sample were also identical. The solubility of the different drug samples was also found to be similar to that of standard. Contrary to individual standards no change in the wavelengths of the matching samples was observed.

Table.7. Preformulation studies of α-Tocopherol

Sr. No	Parameters	Standard	Sample
1	Melting Point	2.5-3.5^{0}C	3.1^{0}C
2	Appearance	Pale yellow to amber, viscous oily liquid	Pale yellow viscous liquid
3	Solubility	Insoluble in water, freely soluble in ethanol, ether, acetone, chloroform and oils	Complies
4	Wavelength	292nm	291nm

4.1.4 Solubility studies Alpha Tocopherol

It was clear from the solubility studies that α-tocopherol showed high solubility in ethanol in contrast to other solvents.

Table.8. Solubility study of drug in different solvents

Sr. No	Solvents	Solubility of Alpha Tocopherol
1	Water	+
2	Ethanol	+++
3	Methanol	++
4	Buffer	+

Highly soluble +++, Soluble ++, poorly soluble +

4.1.5 Determination of maximum wavelength (λmax)

The λmax of Curcumin was found to be 420nm which is in agreement with the standard drug. The maximum absorbance is shown in the figure below and the graph.

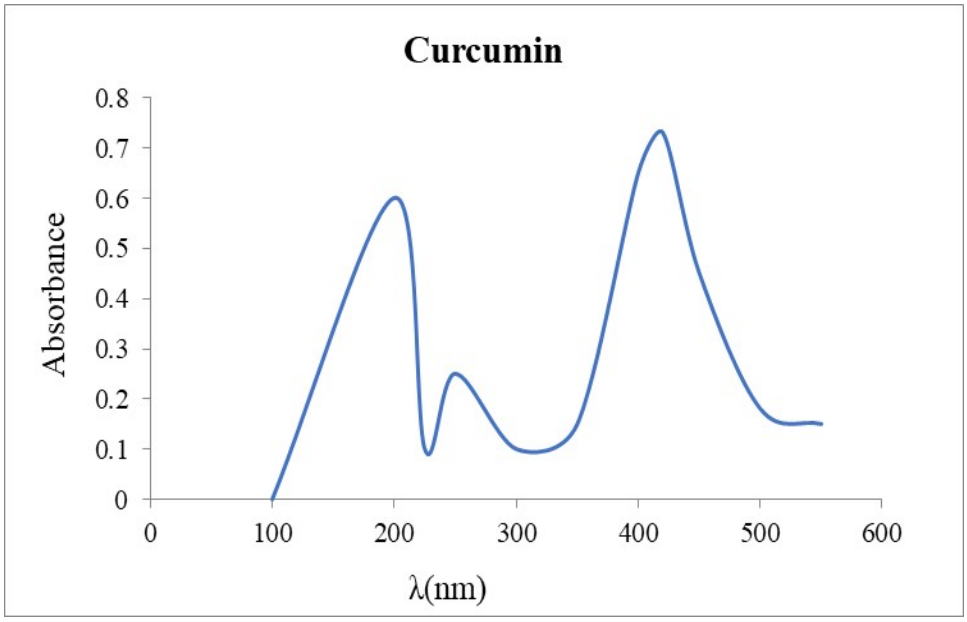

Figure.9. Absorption maxima (λmax) of curcumin at 420 nm

4.1.6 Standard calibration curve

Curcumin standard curves were prepared in a buffer solution at pH 6.8 with different concentrations. Absorption was seen at 2, 4, 6, 8 and 10 ug/ml. Also, the regression coefficient was calculated and found to be near to unity, which indicates that the standard graphs can be used for further study.

Table.9. Absorbance of curcumin at different Concentration

Sr. No	Concentration (µg/ml)	Absorbance @290 nm
1.	2µg/ml	0.154
2.	4µg/ml	0.318
3.	6µg/ml	0.427
4.	8µg/ml	0.585
5.	10µg/ml	0.781

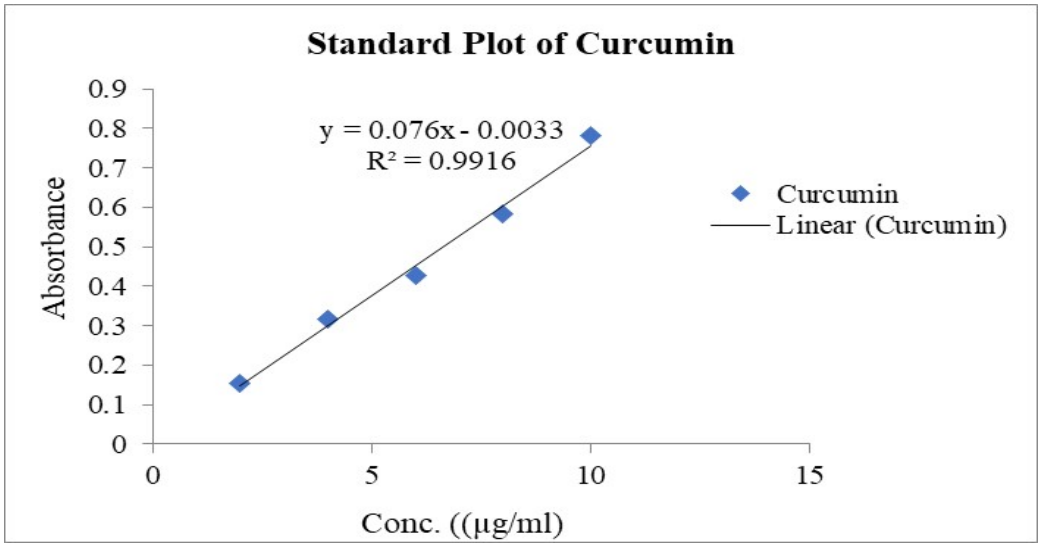

Figure.10. Standard calibration curve of Curcumin

4.1.7 Determination of maximum wavelength (λmax)

The maximum wavelength (λmax) for curcumin was 290nm in accordance with the standard drug. The figure below shows the maximum absorbance and the graph.

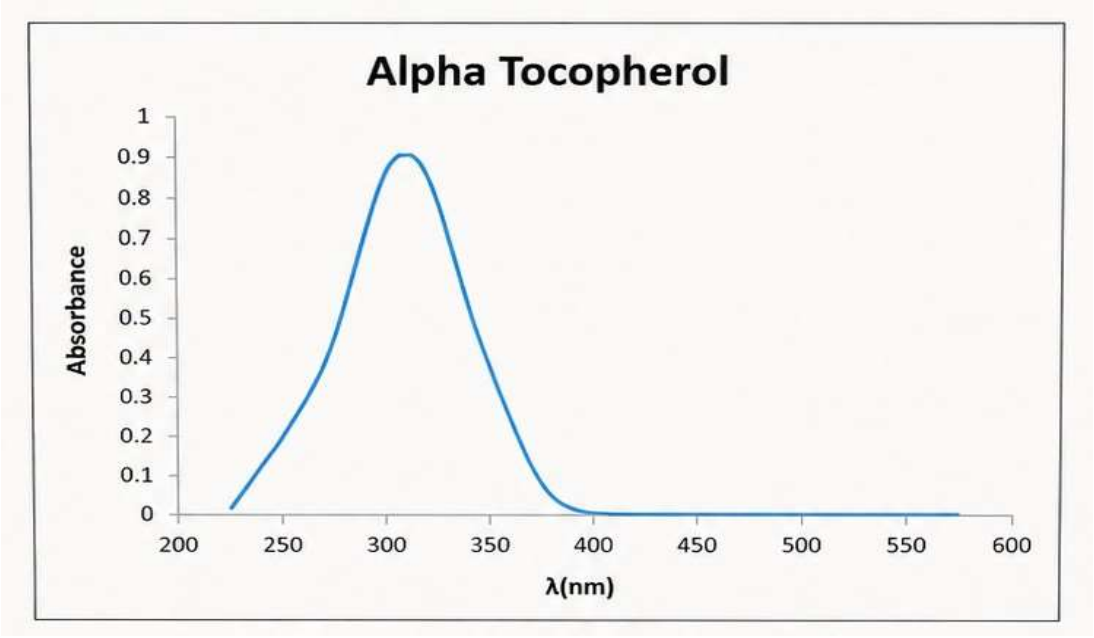

Figure.11. Absorption maxima (λmax) of α-tocopherol (292 nm)

4.1.8 Standard calibration curve

The standard curve of Alpha Tocopherol was developed using different concentrations of ethanol. Absorption was observed at concentrations of 2, 4, 6, 8 and 10 µg/ml. Also, the regression coefficient was calculated and found to be near to unity, which indicates that the standard graphs can be used for further study.

Table.10. Absorbance of α-tocopherol at different Concentration

Sr. No	Concentration (µg/ml)	Absorbance @292 nm
1.	2µg/ml	0.142

2.	4µg/ml	0.279
3.	6µg/ml	0.399
4.	8µg/ml	0.579
5.	10µg/ml	0.711

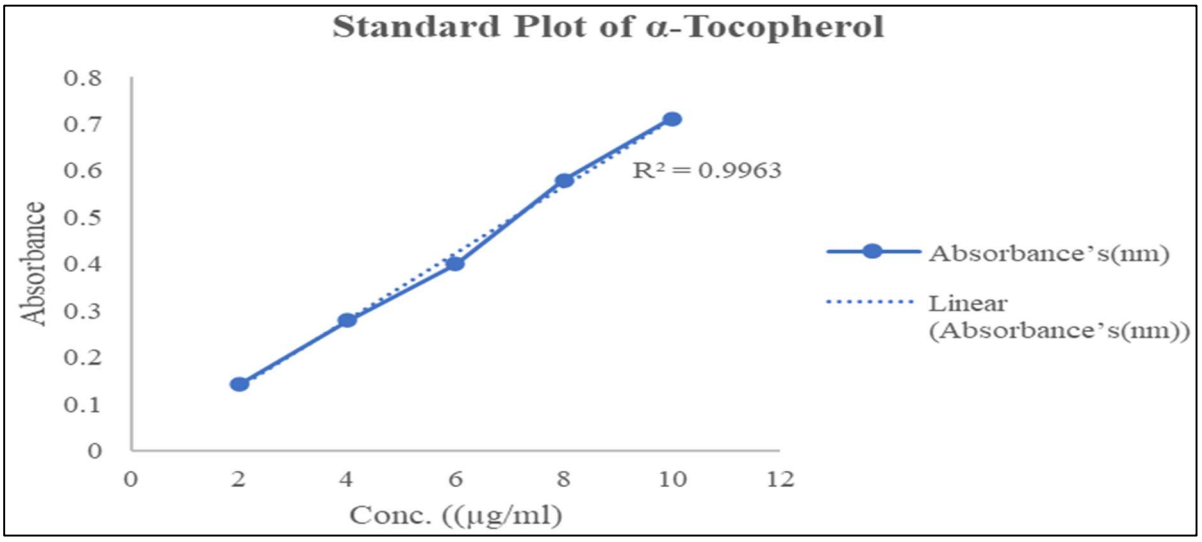

Figure.12. Standard calibration curve of α-tocopherol

4.2 Evaluation of Topical formulations

4.2.1 Physical and Pharmaceutical parameters

All the developed formulations were found to be smooth, greasy and white in color with characteristic odour.

The studies showed that F3 formulation complies with requirements of physical parameters and likewise found to be the best amongst all the batches ***(Table No.11).*** From here onwards we used F3 formulation for further analysis.

Table.11. Physical and Pharmaceutical parameters of cream base

Parameter	Formulation Code				
	FC1	**FC2**	**FC3**	**FC4**	**FC5**
Appearance	White	White	White	White	White
Odour	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy
Homogeneity	Good	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable	Removable
PH	6.2	5.8	5.8	6.5	6.5
Viscosity	424000cp	518000cp	256200cp	841000cp	936000cp
Spreadability	2.27	4.46	10.86	2.21	2.42

The studies showed that F2 formulation complies with requirements of physical parameters and likewise found to be the best amongst all the batches ***(Table No.12).*** From here onwards we used F3 formulation for further analysis.

Table.12. Physical and Pharmaceutical parameters of Gel base

Parameter	Formulation Code				
	FG1	**FG2**	**FG3**	**FG4**	**FG5**
Appearance	Clear gel	Clear gel	Clear gel	Clear gel	Clear gel
Odour	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy
Homogeneity	Good	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable	Removable
PH	6.2	5.2	5.8	6.5	6.5
Viscosity	24,100cp	36,200	48,500cp	54,000cp	68,900cp
Spreadability	5.26	3.82	2.85	2.37	1.63

The developed formulations were found to be smooth, non-greasy, white and yellow in colour with characteristic odour.

Table No. 13. Physical and Pharmaceutical parameters of cream (F3+drug)

Parameter	Formulation Code			
	FC3	**FC3 + α-Tocopherol**	**FC3 + Curcumin**	**FC3 + α-Tocopherol + Curcumin NLC**
Appearance	White	White	Yellow	Yellow
Odor	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy
Homogeneity	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable
PH	5.8	6.2	5.8	6.1
Viscosity	256,100cp	257,400cp	262,000cp	271,200cp
Spreadability	10.86	7.35	8.06	8.81

Table No. 14. Physical and Pharmaceutical parameters of Gel (F2+drug)

Parameter	Formulation Code			
	FG2	**FG2+ α-Tocopherol**	**FG2 + Curcumin**	**FG2 + α-Tocopherol + Curcumin NLC**
Appearance	Clear	Clear	Pale Yellow	Pale Yellow
Odor	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy

Homogeneity	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable
PH	6.2	5.8	5.8	6.5
Viscosity	36,200cp	36,800cp	37,400cp	39,300cp
Spreadability	3.82	4.15	4.53	5.02

4.2.2 In-vitro drug release studies

In-Vitro Release of Topical Formulation Containing Curcumin NLC and α-Tocopherol

Franz diffusion cell was used to study drug release pattern. Graph was plotted in between %CDR and time.

It was observed from the graph that the free drug was released within minutes of time interval whereas the constant and slow release of drug was observed in formulated cream for 8 hrs and no release was found in the blank formulation.

Table.15. % Cumulative drug release (CDR) of Curcumin and α-Tocopherol in Topical formulations

Time (h)	% Drug Released (CNL)	% Drug Released (CNL-loaded cream)	% Drug Released (CNL-loaded Gel)
0	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
1	15.4 ± 0.7	8.40 ± 0.3	9.2 ± 0.5
2	25.3 ± 1.0	14.8 ± 0.6	18.3 ± 0.8
3	34.6 ± 1.2	23.1 ± 0.5	28.5 ± 1.1
4	45.7 ± 1.4	29.5 ± 0.9	35.8 ± 1.3
5	55.2 ± 1.6	37.1 ± 1.2	46.1 ± 1.5
6	63.9 ± 1.8	46.3 ± 1.3	52.6 ± 1.7
7	71.4 ± 1.9	51.7 ± 1.6	61.9 ± 1.8
8	78.1 ± 2.1	63.4 ± 1.9	68.2 ± 2.0

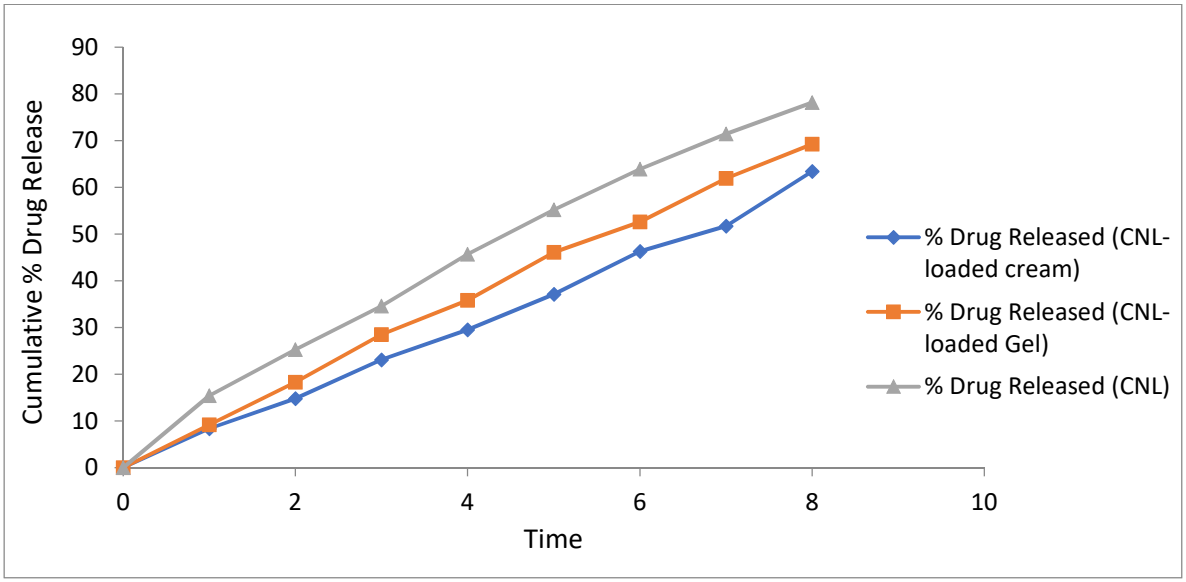

Figure.13. Graphical representation of %Drug release

4.2.3 Stability Studies of Cream

The stability studies were performed on the formulation at different temperatures [40C and room temperature] with closed lid for 60 days and various parameters were taken into consideration to check the stability of the cream. The observation depicted in the tables at different temperature and with closed and open *lid* ***(Table No. 16-19)***. No change in the pH was observed throughout the study. Small change in the viscosity and Spreadability studies was observed with the time.

Table.16. Stability Studies of cream (FC3 + α-Tocopherol + Curcumin NLC) at 40C

Parameters	Day 1	Day 15	Day 30	Day 45	Day 60
Appearance	Yellow	Yellow	Yellow	Yellow	Yellow
Odor	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy
Homogeneity	Good	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable	Removable
PH	5.6	5.6	5.7	5.7	5.7
Viscosity	273000cp	284000cp	297000cp	317000cp	341000cp
Spreadability	8.54	7.79	6.64	5.81	3.97

Table.17. Stability Studies of Gel (FG2 + α-Tocopherol + Curcumin NLC) at 40C

Parameters	Day 1	Day 15	Day 30	Day 45	Day 60
Appearance	Yellow	Yellow	Yellow	Yellow	Yellow
Odor	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy
Homogeneity	Good	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable	Removable
PH	5.6	5.6	5.7	5.7	5.7
Viscosity	39100cp	43400cp	47300cp	55200cp	63900cp
Spreadability	4.96	4.38	3.76	3.15	2.29

Table.18. Stability Studies of cream (FC3 + α-Tocopherol + Curcumin NLC) at room temperature

Parameters	Day 1	Day 15	Day 30	Day 45	Day 60
Appearance	Yellow	Yellow	Yellow	Yellow	Yellow
Odor	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy
Homogeneity	Good	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable	Removable

PH	5.6	5.6	5.7	5.7	5.7
Viscosity	271,100cp	258,000cp	224,700cp	203,100cp	196,800cp
Spreadability	8.76	8.84	9.13	9.47	9.83

Table.19. Stability Studies of Gel (FG2 + α-Tocopherol + Curcumin NLC) at room temperature

Parameters	Day 1	Day 15	Day 30	Day 45	Day 60
Appearance	Yellow	Yellow	Yellow	Yellow	Yellow
Odor	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth	Smooth	Smooth	Smooth	Smooth
Greasiness	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy	Non-Greasy
Homogeneity	Good	Good	Good	Good	Good
Removal	Removable	Removable	Removable	Removable	Removable
PH	5.6	5.6	5.7	5.7	5.7
Viscosity	39200cp	38400cp	36800cp	35200cp	33900cp
Spreadability	5.16	5.43	5.79	5.94	6.26

4.2.4 Antibacterial Activity of Curcumin–α-Tocopherol-Loaded NLC Gel and Cream

The antibacterial activity of the Curcumin–α-Tocopherol-loaded NLC gel and NLC cream was evaluated against Escherichia coli and Staphylococcus aureus. Both formulations exhibited significant antibacterial activity compared to the blank formulations, confirming the antimicrobial potential of the encapsulated bioactive compounds.

The NLC gel showed greater antibacterial activity than the NLC cream, which may be attributed to its faster drug release and better diffusion through the gel matrix. In contrast, the cream formulation provided a comparatively slower and more sustained release of the encapsulated drugs.

The cup plate method further confirmed these findings, with the NLC gel producing larger zones of inhibition against both bacterial strains than the NLC cream, while the blank formulations showed no inhibition zones. Overall, both formulations demonstrated effective antibacterial activity; however, the Curcumin–α-Tocopherol-loaded NLC gel exhibited superior antimicrobial efficacy, indicating its greater suitability for topical treatment of bacterial skin infections.

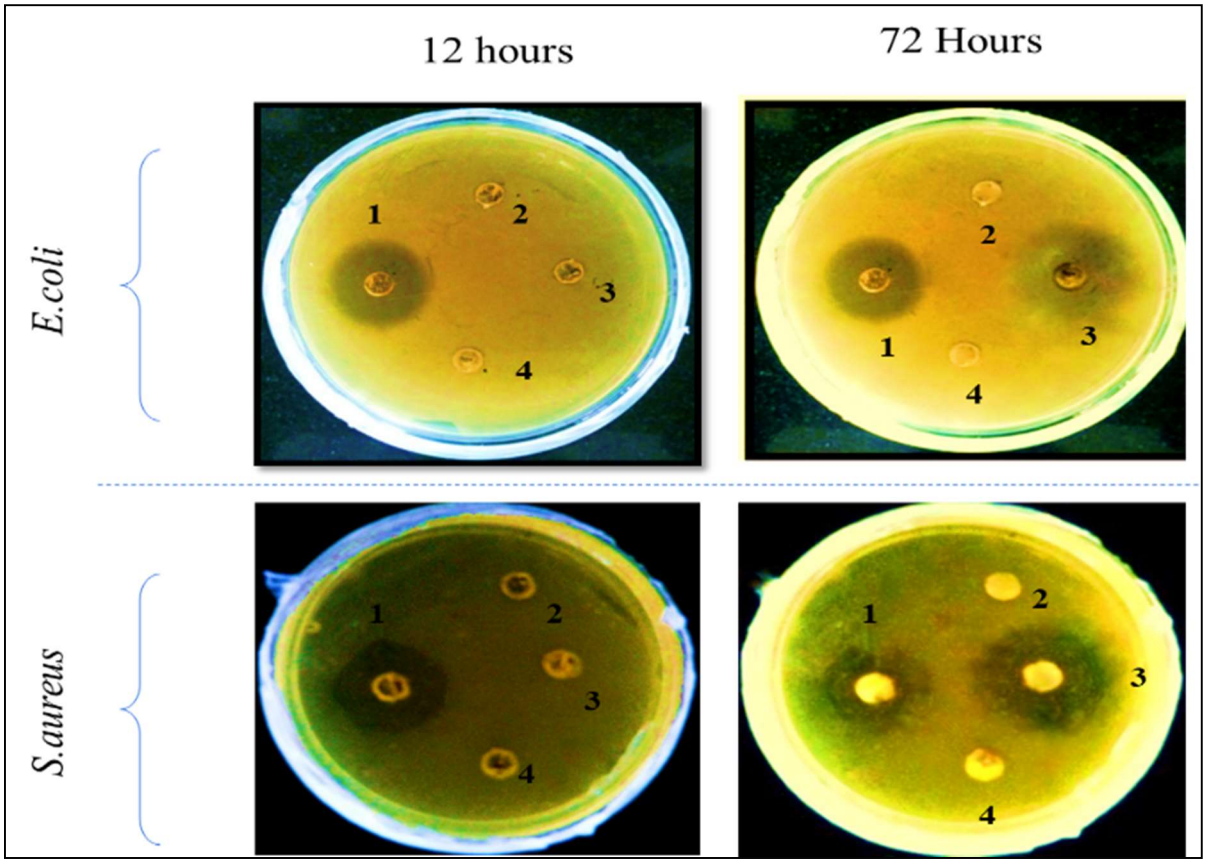

Figure.14. Qualitative growth inhibition assay of bacteria on agar plates with effect on S. aureus & E. coli. with respect to cream formulation

Table.20. Qualitative growth inhibition assay of bacteria on agar plates with effect on E. coli. with respect to cream formulation

+ve Control (cm-diameter)	PBS (cm-/diameter)	Blank-Cream (cm-diameter)	NLCs loaded Cream (cm-diameter)
3cm	0cm	0cm	0cm
3cm	0cm	0cm	3.5cm

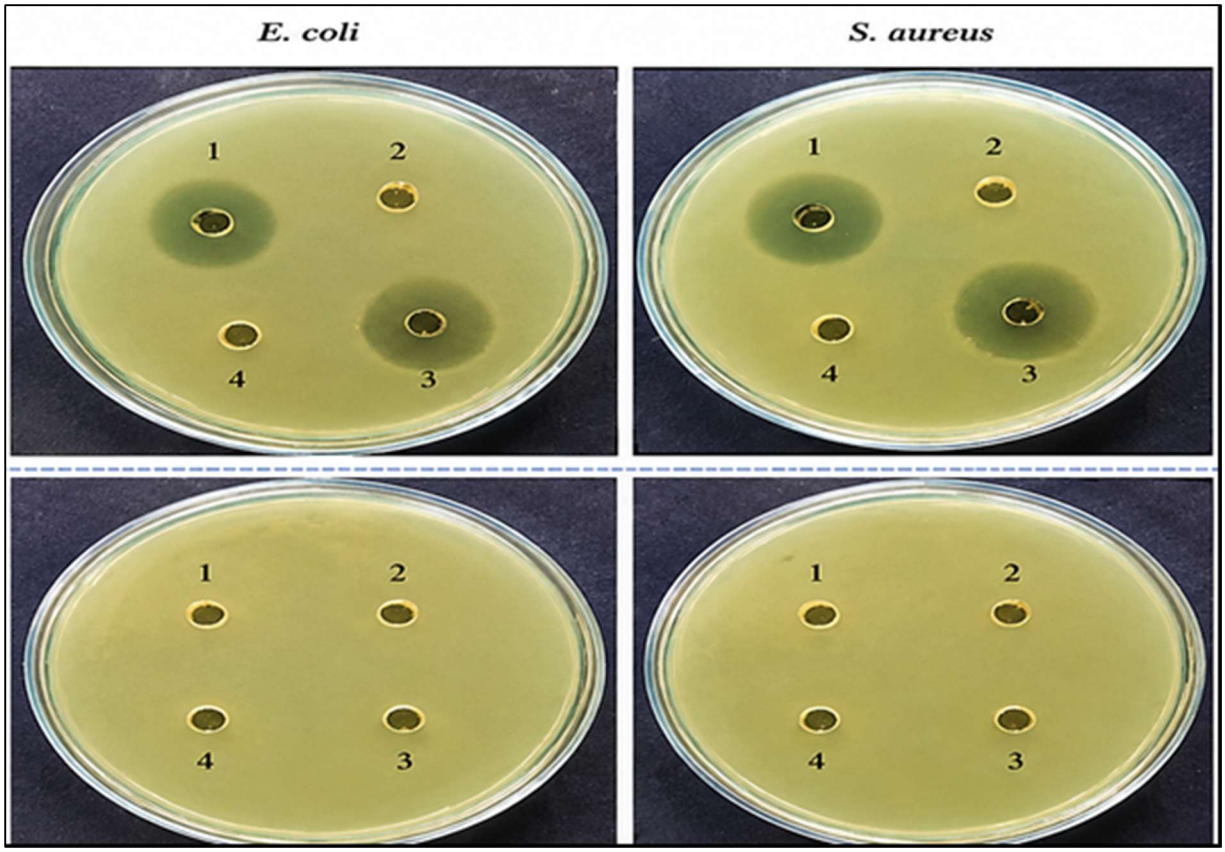

Figure.15. Qualitative growth inhibition assay of bacteria on agar plates with effect on S. aureus & E. coli. with respect to gel formulation

Table.21. Qualitative growth inhibition assay of bacteria on agar plates with effect on E. coli. with respect to gel formulation.

+ve Control (cm-diameter)	PBS (cm-/diameter)	Blank-Gel (cm-diameter)	NLCs loaded Gel (cm-diameter)
3cm	0cm	0cm	0cm
3cm	0cm	0cm	3.8cm

CONCLUSION

The present study successfully developed and optimized Curcumin–α-Tocopherol-loaded Nanostructured Lipid Carriers (NLCs) for topical drug delivery. The optimized NLCs exhibited desirable physicochemical properties, including nanosized particle size, low polydispersity, high encapsulation efficiency, good drug loading, and satisfactory stability. FTIR analysis confirmed the compatibility of Curcumin, α-tocopherol, and formulation excipients without any significant chemical interaction.

The optimized NLCs were successfully incorporated into topical gel and cream formulations, both of which showed acceptable pH, homogeneity, viscosity, spreadability, and stability for dermal application. In vitro drug release studies demonstrated controlled release, with the gel providing faster drug diffusion, while the cream offered a more sustained release profile.

Comparative antibacterial studies against Escherichia coli and Staphylococcus aureus revealed that the NLC-loaded gel exhibited superior antimicrobial activity, whereas the NLC-loaded cream provided better retention and prolonged drug release. Overall, co-encapsulation of Curcumin and α-tocopherol in NLCs significantly improved their stability and therapeutic performance. These findings indicate that both formulations are promising topical delivery systems, with the gel being suitable for rapid antimicrobial action and the cream for sustained therapeutic effects. Future in vivo and clinical studies are recommended to further validate their efficacy.

REFERENCES

1. Nurohman I, Suhandi C, Chaerunisaa AY, Wilar G, Jafar G, Sriwidodo S. Design Evolution of Curcumin-Loaded Nanostructured Lipid Carriers: Formulation Strategies, Functional Modifications, and Mechanistic-Translational Perspectives. Int J Nanomedicine. 2026 Mar 10;21:586727. doi: 10.2147/IJN.S586727. PMID: 41836730; PMCID: PMC12988807.

2. Lim, H.W.; Kohli, I.; Ruvolo, E.; Kolbe, L.; Hamzavi, I.H. Impact of visible light on skin health: The role of antioxidants and free radical quenchers in skin protection. J. Am. Acad. Dermatol. 2022, 86, S27–S37.

3. Jing, Y.; Ruan, L.; Jiang, G.; Nie, L.; Shavandi, A.; Sun, Y.; Xu, J.; Shao, X.; Zhu, J. Regenerated silk fibroin and alginate composite hydrogel dressings loaded with curcumin nanoparticles for bacterial-infected wound closure. Biomater. Res. 2023, 149, 213405.

4. Fu, Y.S.; Chen, T.H.; Weng, L.; Huang, L.; Lai, D.;Weng, C.F. Pharmacological properties and underlying mechanisms of curcumin and prospects in medicinal potential. Biomed. Pharmacother. 2021, 141, 111888.

5. Shah, M.; Murad, W.; Mubin, S.; Ullah, O.; Rehman, N.U.; Rahman, M.H. Multiple health benefits of curcumin and its therapeutic potential. Environ. Sci. Pollut. Res. 2022, 29, 43732–43744.

6. Caddeo, C.; Manca, M.L.; Peris, J.E.; Usach, I.; Diez-Sales, O.; Matos, M.; Fernández-Busquets, X.; Fadda, A.M.; Manconi, M. Tocopherol-loaded transfersomes: In vitro antioxidant activity and efficacy in skin regeneration. Int. J. Pharm. 2018, 551, 34–41.

7. Akhtar, N.; Akhtar, N.; Menaa, F.; Alharbi, W.; Alaryani, F.S.S.; Alqahtani, A.M.; Ahmad, F. Fabrication of ethosomes containingtocopherol acetate to enhance transdermal permeation: In vitro and ex vivo characterizations. Gels 2022, 8, 335.

8. Cheng, H.; Fan, Q.; Liu, T.; Wusigale, L. Co-encapsulation of _-tocopherol and resveratrol in oil-in-water emulsion stabilized by sodium caseinate: Impact of polysaccharide on the stability and bioaccessibility. J. Food Eng. 2020, 264, 109685.

9. 8. Na, Y.; Woo, J.; Choi, W.I.; Lee, J.H.; Hong, J.; Sung, D. _-Tocopherol-loaded reactive oxygen species-scavenging ferrocene nanocapsules with high antioxidant efficacy for wound healing. Int. J. Pharm. 2021, 596, 120205.

10. Jain, H.; Geetanjali, D.; Dalvi, H.; Bhat, A.; Godugu, C.; Srivastava, S. Liposome mediated topical delivery of Ibrutinib and curcumin as a synergistic approach to combat Imiquimod induced psoriasis. J. Drug Deliv. Sci. Technol. 2022, 68, 103103.

11. Farhoudi, L.; Kesharwani, P.; Majeed, M.; Johnston, T.P.; Sahebkar, A. Polymeric nanomicelles of curcumin: Potential applications in cancer. Int. J. Pharm. 2022, 617, 121622.

12. Zheng, B.; McClements, D.J. Formulation of more efficacious curcumin delivery systems using colloid science: Enhanced solubility, stability, and bioavailability. Molecules 2020, 25, 2791.

13. Tabanelli, R.; Brogi, S.; Calderone, V. Improving Curcumin Bioavailability: Current strategies and future perspectives. Pharmaceutics 2021, 13, 1715.

14. Fan, C.; Feng, T.; Wang, X.; Xia, S.; Swing, C.J. Liposomes for encapsulation of liposoluble vitamins (A, D, E and K): Comparation of loading ability, storage stability and bilayer dynamics. Food Res. Int. 2023, 163, 112264. Pharmaceutics 2023, 15, 1912 18 of 19

15. Abla, M.J.; Banga, A.K. Formulation of tocopherol nanocarriers and in vitro delivery into human skin. Int. J. Cosmet. Sci. 2014, 36,239–246.

16. Kerdpol, K.; Nutho, B.; Krusong, K.; Poo-arporn, R.P.; Rungrotmongkol, T.; Hannongbua, S. Encapsulation of alpha tocopherol in large-ring cyclodextrin containing 26-D-glucopyranose units: A molecular dynamics study. J. Mol. Liq. 2021, 339, 116802.

17. Zhang, L.; Lin, Z.; Chen, Y.; Gao, D.; Wang, P.; Lin, Y.; Wang, Y.; Wang, F.; Han, Y.; Yuan, H. Co-delivery of docetaxel and resveratrol by liposomes synergistically boosts antitumor efficiency against prostate cancer. Eur. J. Pharm. Sci. 2022, 174, 106199.

18. Zhang, Z.J.; Michniak-Kohn, B. Flavosomes, novel deformable liposomes for the co-delivery of anti-inflammatory compounds to skin. Int. J. Pharm. 2020, 585, 119500.

19. Preetha Anand, Ajaikumar B. Kunnumakkara, Robert A. Newman, and Bharat B. Aggarwal Molecular Pharmaceutics 2007 4 (6), 807-818 DOI: 10.1021/mp700113r

20. Mahdi WA, Bukhari SI, Imam SS, Alshehri S, Zafar A, Yasir M. Formulation and optimization of butenafine-loaded topical nano lipid carrier-based gel: characterization, irritation study, and anti-fungal activity. Pharmaceutics. 2021 Jul 16;13(7):1087.

21. Uprit S, Sahu RK, Roy A, Pare A. Preparation and characterization of minoxidil loaded nanostructured lipid carrier gel for effective treatment of alopecia. Saudi Pharmaceutical Journal. 2013 Oct 1;21(4):379-85.

22. Pandey, B., Subedi, L., &Baral, R. (2022). Formulation and Invitro Characterization of AceclofenacEmulgel Prepared using Carbopol 934 and

Sodium CMC.Journal of Natural &Ayurvedic Pharmacy and Drug Discovery, July 2022.

23. Rompicherla, N. C., Joshi, P., Shetty, A., Sudhakar, K., Amin, H. I., Mishra, Y., Mishra, V., Albutti, A., &Alhumeed, N. (2022). Design, Formulation, and Evaluation of Aloe vera Gel-Based Capsaicin Transemulgel for Osteoarthritis. Pharmaceutics, 14(9), 1812 https://doi.org/10.3390/pharmaceutics14091812

24. Manian, M., Jain, P., Vora, D., & Banga, A. K. (2022). Formulation and Evaluation of the In Vitro Performance of Topical Dermatological Products Containing Diclofenac Sodium. Pharmaceutics, 14(9), 1892. https://doi.org/10.3390/pharmaceutics14091892

25. Ali Khan, B., Ullah, S., Khan, M., Alshahrani, S. M., & Braga, V. A. (2020). Formulation and evaluation of Ocimumbasilicum-based emulgel for wound healing using animal model. Saudi Pharmaceutical Journal, 28(12), 1842-1850. https://doi.org/10.1016/j.jsps.2020.11.011

26. Kukreja, T., & Saraf, S. (2023). Formulation of Topical Itraconazole Nanostructured Lipid Carriers (NLC) Gel for Onychomycosis. Journal of Ravishankar University (PART-B), 35(2), 8-18. https://doi.org/10.52228/jrub.2023-35-2-2

27. Singh Chauhan, Y., Nex, R., Sevak, G., & Singh Rathore, M. (2021). Stability testing of pharmaceutical products. Research Journal of Pharmaceutical Dosage Forms and Technology, 13(4), 317-328. https://doi.org/10.52711/0975-4377.2021.00052

28. Yuan H, Wang LL, Du YZ, et al. Preparation and characteristics of nanostructured lipid carriers for control-releasing progesterone by melt-emulsification. Colloids Surf B Biointerfaces 2007; 60: 174–179.

29. Singh S, Kushwaha AK, Vuddanda PR, et al. Development and Evaluation of Solid Lipid Nanoparticles of Raloxifene Hydrochloride for Enhanced Bioavailability. Biomed Res Int 2013; 2013: 584549.