

Design and Optimization of a Tazarotene-Containing Emulgel for the Treatment of Acne

Amit Pratap Singh, Sakshi Soni, Poornima Agrawal, Vandana Soni*

Department of Pharmaceutical Sciences

Dr. Harisingh Gour Vishwavidyalaya, Sagar, Madhya Pradesh, 470003

E-mail: vsoni@dhsu.edu.in

(Received on 22/10/2022; Accepted on 05/12/2022)

Abstract

This study aimed to formulate a stable emulgel containing Tazarotene and assess its effectiveness in treating acne, as well as its antibacterial activity. To develop the emulgel formulation, Cinnamon oil, and Triethanolamine were used. The antibacterial effect of the Tazarotene drug was assessed using the agar diffusion method. The developed emulgel formulation showed a pH of 6.8, spreadability of 6.17 ± 0.02 cm, a viscosity of 28886 ± 2.37 cps, and drug content of $85.46\% \pm 0.03\%$. The emulgel formulation's stability study revealed that it remained stable for more than 30 days at both $4 \pm 1^\circ\text{C}$ and room temperature. The antibacterial study showed that the emulgel formulation with Tazarotene had a zone of inhibition of 30mm, while the emulgel formulation without Tazarotene and with Cinnamon Oil had an inhibition zone of 9mm. The emulgel formulation without Tazarotene and Cinnamon Oil did not show any zone of inhibition. The results of the above studies indicated that the prepared formulation is more efficient for the treatment of acne.

Keywords: Tazarotene, Cinnamon Oil, emulgel formulation, acne, antibacterial activity.

Introduction

Acne vulgaris is a prevalent skin disorder that impacts an estimated 650 million individuals globally, primarily affecting adolescents with the highest incidence rate. The condition can cause a range of inflammatory and noninflammatory lesions, including papules, pustules, nodules, and comedones, as well as scarring. Acne occurs primarily in areas with a high density of pilosebaceous units, Common areas affected by acne include the face, neck, chest, shoulders, and back. While acne is often considered a minor cosmetic concern, it can have significant impacts on quality of life, including anxiety, social withdrawal, and depression. The management of acne involves various treatment options, including both topical and systemic therapies. These treatment options comprise retinoids, benzoyl peroxide, azelaic acid, antibiotics, and systemic retinoids. Hormone therapy and oral contraception are also recommended for women with acne, particularly when isotretinoin is contraindicated or ineffective, or when there are signs of ovarian or adrenal hyperandrogenism. Topical retinoids are among the most commonly prescribed treatments for acne, as they are effective in both treating and preventing the condition (Ahmad *et al.*, 2023, Miaset *et al.*, 2023, Pawar *et al.*, 2023 and Arooj *et al.*, 2023). Nonetheless, conventional topical formulations, such as creams, ointments, and lotions, have certain disadvantages, including stickiness and poor spreading coefficient, which can lead to discomfort and reduced efficacy. Emulgel is a novel formulation that combines the advantages of both emulsions and gels, offering a more efficient drug delivery system for lipophilic and hydrophobic drugs. Emulgel is made by combining an oil-in-

water and a water-in-oil emulsion with a gel. It offers many benefits, such as thixotropy, easy spreadability, emollience, and long shelf-life, while also being bio-friendly and cosmetically acceptable (Garget *et al.*, 2016 and Common *et al.*, 2019). The properties of emulsion and gel preparations are distinct, but emulgel overcomes the limitations of gels for hydrophobic drug delivery. Emulsions can be transformed into emulgel by incorporating a gelling agent. In the field of cosmetics and pharmaceuticals, transparent gels are preferred over semisolids such as ointments, creams, and lotions due to their disadvantages like stickiness, less spreading abilities, and the need for rubbing during application. However, one major drawback of gels is their inability to incorporate and deliver hydrophobic drugs through the aqueous gel base. To address this issue, a unique approach of utilizing emulgel formulation can be adopted to incorporate hydrophobic drugs into an aqueous gel base. Emulgels are emulsions of oil-in-water or water-in-oil that have been gelled by combining with a gelling agent. They possess the characteristics of both gels and emulsions and serve as dual control release systems (Xiang *et al.*, 2023).

Tazarotene (TZA) is a receptor-selective synthetic acetylenic retinoid that has been shown to have a strong inhibitory effect on keratinocyte proliferation and differentiation, with clinically significant comedolytic activity. It is used to treat acne, psoriasis, and photoaging (Badawi *et al.*, 2023). When tazarotene is applied, it quickly hydrolyzes to its main metabolite, tazarotenic acid, which binds to retinoic acid receptors (RARs) in the nucleus. The affinity of Tazarotenic acid is specific to RARs, with low affinity towards retinoid X receptors. RAR is the most frequently expressed type of RAR

in the human epidermis, suggesting its crucial role as a mediator of retinoid action in the skin. Tazarotene aids in normalizing abnormal keratinocyte differentiation, decreasing epidermal hyperproliferation, and regulating gene transcription. It was hypothesized that Tazarotene-loaded SLNs and NLCs would exhibit enhanced anti-psoriatic activity when compared to commercially available formulations. However, prolonged treatment duration of weeks or months may result in adverse reactions such as pruritus, burning or stinging sensations, and erythema, which can affect a considerable number of users. Therefore, the application of Emulgel vehicles to the skin could gradually distribute the anti-acne agent(s) and potentially reduce irritancy. These formulations have also been reported to facilitate follicular targeting, leading to increased local concentrations of the active ingredient in the pilosebaceous unit and improved penetration into hair follicles (Parmar *et al.*, 2019). Thus, emulgel could play a critical role in improving the topical delivery of anti-acne agents by improving dermal localization while reducing adverse effects. Furthermore, emulgels known to deliver drugs more quickly than conventional formulations, which can frequently lead to the interruption or discontinuation of the treatment regimen. The poor solubility of tazarotene and its associated tolerability issues have posed a challenge for its formulation in a suitable vehicle, leading to either treatment non-compliance or discontinuation in patients. The emulgent formulation will provide the long release of the drug at the site of action and cinnamon oil provides a synergistic effect for the treatment of acne. Therefore, the development of an effective and tolerable emulgel vehicle for tazarotene could significantly improve patient compliance and treatment outcomes.

Materials and Method

In this study, the Tazarotene (TAZ) sample was obtained as a gift from Glenmark Pharmaceuticals Ltd. located in Nasik, India. The materials used in the experiment, including media (Brain heart infusion, BHI) Span 80, Tween 80, Light liquid paraffin, propylene glycol, methyl paraben, propyl paraben, Carbopol 940, and cinnamon oil, were procured from authentic brands. The bacterial strain *P. acne* was purchased from MTCC located in Chandigarh, India. All of the reagents

and solvents used in this study were of analytical grade, and distilled water were used throughout the experiment.

Formulation of Emulgel

Oil Phase Preparation: Weigh and measure the specified quantities of light liquid paraffin, Span 80, and Cinnamon oil as defined in Table 1. Dissolve Span 80 in light liquid paraffin in a clean, dry container, ensuring thorough mixing. Heat the oil phase to a temperature range of 70-80°C and maintain this temperature throughout the process.

Aqueous Phase Preparation: In a separate container, measure the specified ratios of Tween 80, Propylene glycol, Methyl Paraben, and Propyl Paraben according to Table 1. Dissolve these ingredients in purified water until complete dissolution is achieved. Heat the aqueous phase to the same temperature range of 70-80°C as the oil phase.

Emulsion Formation: With both the oil and aqueous phases at the specified temperature range, gently pour the oil phase into the aqueous phase while stirring continuously to create an oil-in-water (o/w) emulsion. Continue stirring (Speed 500 to 1000 rpm) until the emulsion is homogeneous (Parmar *et al.*, 2019).

Adjust the pH of the emulsion to the target range of 6 to 7 using Triethanolamine (TEA). Gradually add TEA while monitoring the pH using a pH meter until the desired pH level is reached. Allow the emulsion to cool to room temperature while gently stirring. This cooling process is essential for stabilizing the emulsion. Introduce Carbopol 940, serving as the gelling agent, into the emulsion. The weight ratio of Carbopol 940 to the emulsion should be 1:1. Stir moderately but thoroughly to ensure even distribution of the gelling agent throughout the formulation. Continue stirring until the emulgel formulation is smooth, homogeneous, and possesses the desired aesthetic properties. The stirring speed and duration should be sufficient to achieve this. After achieving a uniform emulgel formulation, prepare it for packaging. Store the formulation in appropriate containers, ensuring that the product is protected from environmental contaminants. The formulations can be prepared in different ratios of the listed ingredients, as indicated in Table 1 and prepared formulations are shown in Fig 1. To optimize the formulation for uniformity, spreadability, aesthetic value, and other specific criteria, various combinations of these ingredients can be tested.

Table 1: Composition of different formulation batches (% w/w)

Formula	F1	F2	F3	F4	F5	F6	F7	F8	F9
Tazarotene	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Light Liquid Paraffin	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Span 80	3.2	2.5	2.3	3.2	2.5	2.3	3.2	2.5	2.3
Tween 80	1.8	2.5	2.7	1.8	2.5	2.7	1.8	2.5	2.7
Propylene glycol	5	5	5	5	5	5	5	5	5
Cinnamon oil	8	8	8	8	8	8	8	8	8
Methyl Paraben	0.003	0.003	0.003	0.003	0.003	0.003	0.003	0.003	0.003
Propyl Paraben	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Carbopol 940	0.50	0.75	1.0	1.0	0.50	0.75	0.75	1.0	0.50
Purified water	qs to 100 ml								
Triethanolamine	qs to adjust pH to 6 to 7								

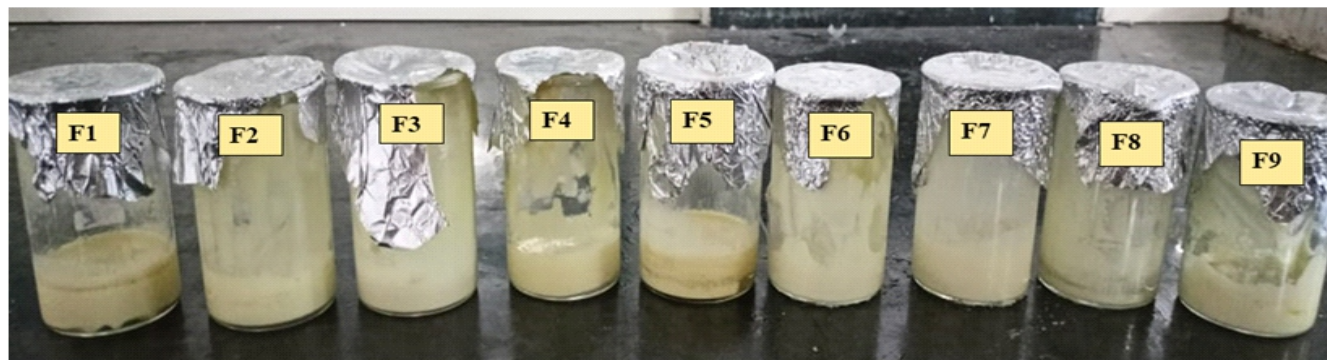


Figure 1: Formulated Emulgels F1 to F9

Characterization of the formulated emulgel

The formulated emulgel was subjected to physical assessment, including visual inspection for color, homogeneity, consistency, and phase separation. further characterized for following parameters.

pH determination

The determination of pH is a critical parameter for topical formulations to avoid significant skin irritation, and the pH of the 1% aqueous solution of Emulgel was measured using a pH meter(Chodankar *et al.*, 2020 and Goyaniet *et al.*, 2018). The results of these studies are shown in Table 2.

Determination of Viscosity

The rheological properties of the emulgel were evaluated using a Brookfield viscometer with spindle number S-64 at various speeds. Such assessments are crucial to ensure that the emulgel is of high quality and efficacy for its intended application (Chodankar *et al.*, 2020). The obtained results are shown in Table 2. All the experiments are done in triplicate.

Optical Microscopy

The morphology of the emulgel was analyzed using a fluorescence microscope at 40x magnifications. A 1% w/w solution of Emulgel in phosphate buffer (pH 6.8) was prepared and sonicated for 10 minutes, then observed under the fluorescence microscope and photographs are shown in Fig 2.

Spreadability

The spreadability of Emulgel was evaluated using specific equipment developed for this purpose. The spreading coefficient was calculated using the Slip and Drag properties and a ground glass slide mounted on a wooden block(Olayemi *et al.*, 2023). The results of spreadability are shown in Table 3.

Emulgel Extrudability

Within the Gel Extrusion Test Procedure for Emulgel formulations F1 to F9, the extrusion test evaluates the rate at which a specific weight of emulgel is dispensed from a tube, measured in grams per second. The process entails emulgel placement in an aluminum tube, secured between glass slides, with a weight added on one slide, and subsequent opening of

the tube cap. Extrudability is gauged by the force necessary to extrude at least 0.5 cm of emulgel within 10 seconds; higher force requirements indicate reduced extrudability. Each formulation's extrudability is tested three times, and the average value is documented. The calculation for extrudability involves dividing the applied weight in grams by the tube opening's area in square centimeters (Chodankar *et al.*, 2020, Goyaniet *et al.*, 2018 and Baibhav *et al.*, 2012). The test was performed in triplicate, and the average values were recorded in Table 4.

$$\text{Extrudability} = \frac{\text{Applied weight (g)}}{\text{Area of the tube opening (cm}^2\text{)}}$$

Swelling index

The swelling capacity of the formulated emulgel was assessed by placing 1 g of gel on a porous aluminum foil and immersing it in a 50 mL beaker containing 10 mL of 0.1 N sodium hydroxide. Samples were then removed from the beakers at different time intervals and placed on a dry surface for a while before being reweighed (Khuntet *et al.*, 2012 and Ambala *et al.*, 2015). The results of the swelling index are shown in Table 5.

Determination of Drug Content

To determine the drug content, 1 g of the emulgel formulation was diluted in a 6.8 pH buffer solution and filtered for clarity. The resulting solution was analyzed for absorbance using a UV-visible spectrophotometer at λ_{max} 351nm after appropriate dilution (Khuntet *et al.*, 2012 and Chodankar *et al.*, 2020). The drug content was then calculated using the following formula:

$$\text{Drug Content} = (\text{Concentration} \times \text{Dilution Factor} \times \text{Volume taken}) \times \text{Conversion Factor}$$

The concentration and volume taken were determined from the UV-visible spectrophotometer readings, while the dilution factor and conversion factor were pre-determined values. The results are shown in Fig 3.

In vitro drug release

To evaluate the in vitro release behavior of the drug from the emulgel formulations, diffusion studies were conducted. A permeation membrane consisting of a dialysis membrane immersed in pH 6.8 phosphate buffer was used. One gram of

the prepared emulgel was uniformly spread on the dialysis membrane, which was then attached to a hollow diffusion tube open on both sides. The receptor compartment was filled with 100 mL of phosphate buffer pH 6.8, which was continuously stirred at 50 rpm using a magnetic stirrer and maintained at a constant temperature of 37 ± 1 °C. Samples of 1 mL were withdrawn from the receptor compartment at 1-hour intervals and replaced with fresh medium. These experiments were conducted to assess the release kinetics of the drug from the emulgel formulation. The amount of Tazarotene released was determined by measuring absorbance at 351 nm using a UV spectrophotometric technique, with pH 6.8 phosphate buffer as a blank (Olayemi *et al.*, 2023; Chodankar *et al.*, 2020). The results of different formulations and optimized formulations in comparison with plain drugs were recorded in Table or Fig4. Based on the characterization parameter the formulation F6 was used for further antibacterial study.

Ex vivo studies: Zone of inhibition (ZOI)

The *ex vivo* study aimed to assess the antibacterial efficacy of tazarotene against *P. acnes* bacteria and to identify the most suitable formulation for subsequent investigations. *P. acnes*, a Gram-positive bacterium, is the primary cause of acne vulgaris, and while tazarotene is a commonly prescribed retinoid medication for acne treatment, its antibacterial properties against *P. acnes* have not been thoroughly studied. The antibacterial potential of tazarotene was evaluated using the well/disc diffusion method, testing various formulations, including plain tazarotene solution, the optimized emulgel formulation F6, an emulgel formulation without the drug and cinnamon oil, and an emulgel formulation without the drug (Charde *et al.*, 2014). The results showed that the emulgel formulation F6 exhibited the most extensive zone of inhibition against *P. acnes*, making it the choice for further investigation like *in vivo* studies in the future. The results are shown in Fig 5.

Results

The formulation and drug selection in this study were motivated by the prevalence of acne, a common dermatological disorder in adolescents, characterized by various skin issues. Acne treatment typically involves a range of medicines, and tazarotene, a retinoid medication, was selected due to its relevance in acne treatment and the need for further exploration of its antibacterial properties against *P. acnes*. The problem addressed is the limitations of existing topical dermatological products, such as ointments and creams, which can be sticky, challenging to spread, and may lack stability. The aim was to develop an emulsion-based emulgel that overcomes these limitations for the effective delivery of both hydrophilic and hydrophobic drugs. The composition of different formulations denoted as F1 to F9, involved a combination of ingredients, including tazarotene, light liquid paraffin, Span 80, Tween 80, propylene glycol, cinnamon oil, methyl paraben, propyl paraben, Carbopol 940, purified water, and Triethanolamine, with varying ratios to characterize the formulation for the desired properties. The characteristics in the studies included the selection of

parameters like pH range, viscosity, spreadability, extrudability, swelling index, and drug content. Formulation F6 was identified as the most promising formulation and further utilized for the study of antibacterial activity against *P. acnes*.

Characterization of Emulgel Formulations

The consistency of all formulated batches of Emulgel was homogeneous, and milky, and exhibited a yellowish-white, creamy appearance with a smooth, homogeneous texture, and free from gritty particles. Ingredients used for the formulated Emulgel are presented in Table 1. The pH of the emulgel formulations was measured by pH meter and observed to be within the normal pH range of the skin, ranging from 6.2 to 6.8. The obtained pH indicated that the prepared formulation will not produce any irritation reaction on the skin. No significant changes in the pH value were observed over time in any of the formulations. The viscosity of the prepared Emulgel formulations (F1-F9) was measured using a Brookfield Viscometer at different rotational speeds (10, 20, 30, 40, 50, 60, 70, 80, 90 rpm), and the viscosity values at 30 rpm were found to range from 24,660 to 56,580 centipoises (cP), as presented in Table 2. The highest viscosity was exhibited with Formulation F3 (50,700 cP), while the lowest viscosity was exhibited with Formulation F7 (24,660 cP) at 30 rpm. The standard deviation of the viscosity measurements ranged from 1.99 to 3.4, indicating that the viscosity values were consistent across the triplicate measurements. The desired range of viscosity for skin formulation is between 10,000 and 100,000 centipoises (cP), the obtained value of viscosity of formulations indicated that the formulation may be spread easily. The results of this study indicate that the formulated emulgel formulations are suitable for topical application due to their desired viscosity, homogeneous consistency, and smooth texture. The selection of F6 can be reasoned based on its viscosity and pH in comparison to the other formulations. F6 exhibits a moderate viscosity of 28886 ± 2.37 cps, which falls within the range of viscosities seen across the formulations. Additionally, its pH of 6.6 aligns closely with the desired range, offering a balanced acidity level. While other formulations might excel in one aspect, F6 strikes a balance between viscosity and pH, making it a suitable choice. Its viscosity is not too high or too low, and the pH is within an acceptable range, positioning F6 as a favorable option considering both these critical parameters for emulgel formulation.

Table 2: pH range and Viscosity of formulation F1-F9

Formulation code	pH	Viscosity (rpm)
F1	6.5	26760 $\pm$ 2.04
F2	6.8	32640 $\pm$ 2.86
F3	6.7	50700 $\pm$ 3.03
F4	6.8	46160 $\pm$ 1.99
F5	6.2	27010 $\pm$ 2.97
F6	6.6	28886 $\pm$ 2.37
F7	6.5	24660 $\pm$ 2.56
F8	6.3	56580 $\pm$ 3.40
F9	6.7	27990 $\pm$ 2.30

Optical Microscopy

The optical-microscopic evaluations of optimized formulation F6 carried out as part of this study involved a detailed examination of the emulgel formulations. These evaluations revealed the presence of spherical globules within the formulations, as depicted in Figure 1. These spherical globules are indicative of the formation of an emulsion within the gel base. In the context of emulgels, an emulsion is a dispersion of oil droplets within a water-based gel. The spherical globules observed represent these oil droplets suspended within the gel matrix. The successful observation of these globules through optical microscopy is a strong indication that the method employed for the preparation of the emulgel formulations was effective and achieved the desired result. In essence, the presence of these globules signifies the successful incorporation of the oil phase into the gel phase, which is a fundamental characteristic of emulgels. It demonstrates that the emulsion is stable within the gel, and this is a crucial aspect in the development of emulgel formulations, as it ensures that the active components are evenly distributed and will perform their intended functions effectively. This observation through optical-microscopic evaluation confirms that the emulgel preparation method used in this study was indeed successful in achieving the desired emulsion within the gel base, which is a key step in formulating emulgels.

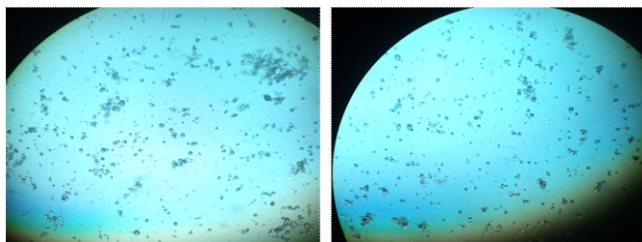


Figure2: Microscopy of optimized Emulgel formulation at 40x magnification

Spreadability Analysis

The spreadability assessment of nine distinct formulations F1 to F9 (F1, 5.54 ± 0.012 cm; F2, 6.02 ± 0.025 cm; F3, 6.12 ± 0.01 cm; F4, 5.40 ± 0.06 cm; F5, 5.89 ± 0.03 cm; F6, 6.17 ± 0.02 cm; F7, 5.70 ± 0.03 cm; F8, 6.15 ± 0.017 cm; and F9, 5.33 ± 0.028 cm) provides valuable insights into their suitability for topical application. Among these formulations, F6 stands out as the most promising candidate, boasting the highest spreadability value at 6.17 ± 0.02 cm. This attribute is instrumental in ensuring easy application, uniform coverage, and enhanced absorption of active ingredients. The assessment of spreadability is important due to its pivotal role in ensuring that topical formulations can be effectively applied and absorbed by the skin, directly impacting the product's therapeutic or cosmetic efficacy. These parameters also greatly influence the overall user experience, as formulations with superior spreadability are more user-friendly and lead to increased user satisfaction and product adherence.

Table 3: Spreadability of formulations F1-F9

Formulation code	Spreadability value (cms)
F1	5.54 ± 0.012
F2	6.02 ± 0.025
F3	6.12 ± 0.01
F4	5.40 ± 0.06
F5	5.89 ± 0.03
F6	6.17 ± 0.02
F7	5.70 ± 0.03
F8	6.15 ± 0.017
F9	5.33 ± 0.028

Gel Extrusion Test

The extrudability values of different emulgel formulations, as presented in Table 4, were measured and recorded. Formulations F3 and F6 exhibited the highest extrudability values, measuring 18 ± 1.39 g/cm² and 18 ± 2.49 g/cm², respectively, indicating their exceptional ease of extrusion. On the other hand, formulations F2, F7, F8, and F9 demonstrated the lowest values, ranging from 14 to 15 g/cm², suggesting relatively less straightforward extrusion. Formulations F1, F4, and F5 fell within the range of 16 to 17 g/cm², showing moderate extrudability. Notably, Formulation F6, with an extrudability value of 18 ± 2.49 g/cm², was identified as the optimized formulation, emphasizing its outstanding suitability for topical application due to its ease of dispensing. This procedure facilitated the quantification of extrudability, a crucial parameter in evaluating the ease of application and user-friendliness of the emulgel formulation.

Table 4: The extrudability values of formulations F1-F9

Formulation code	Spreadability value (cms)
F1	16 ± 2.86
F2	15 ± 2.23
F3	18 ± 2.39
F4	16 ± 2.58
F5	17 ± 2.96
F6	18 ± 2.49
F7	15 ± 2.86
F8	14 ± 2.09
F9	15 ± 2.47

Swelling Index

Table 2 shows the swelling index of formulations F1 to F9 at different time intervals. At the start of the experiment, all formulations had a swelling index of 1. After 15 minutes, the swelling index of most formulations increased slightly, with F4 showing the highest increase (1.30). After 30 and 45 minutes, the swelling index continued to increase, with F6 showing the highest increase (1.40) at 30 minutes, and F9 showing the highest increase (1.40) at 45 minutes. Overall, the formulations showed varying degrees of swelling over time. The swelling index is an important property of emulgels as it indicates how well they can absorb and retain water.

Table 5: Swelling index of formulation F1-F9

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	1	1	1	1	1	1	1	1	1
15	1.20	1.21	1.10	1.30	1.10	1.36	1.17	1.07	1.31
30	1.22	1.28	1.20	1.37	1.11	1.40	1.21	1.19	1.34
45	1.29	1.34	1.15	1.35	1.15	1.46	1.33	1.22	1.40

Drug Content

The drug content of the formulated emulgel was analyzed using spectrophotometry at $\lambda_{\max}$ 351nm, and it was found that the drug content of different emulgel formulations ranged between 78% to 85%. Formulation F6 had the highest drug content 85.46 ± 0.03 % compared to other formulations, indicating its suitability for high entrapment in the internal phase system.

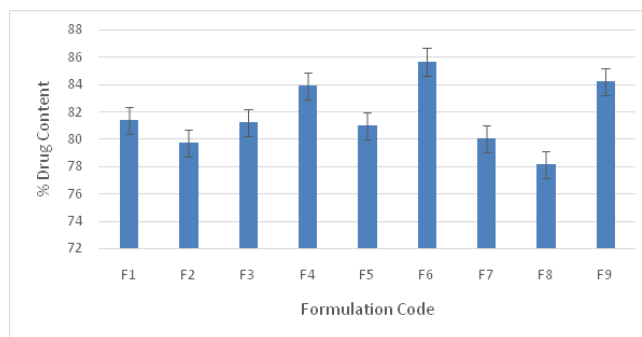


Figure 3: Drug content of formulation F1-F9

In vitro drug release

The *in vitro* release of Tazarotene from the emulgel was dependent on the concentration of the polymer used. The emulgels were evaluated for *in vitro* drug release using phosphate buffer at pH 6.8 for 7 hours. All emulgel formulations showed a good release of the drug, with formulation F6 showing the highest release, followed by F7, F8, F9, F1, F3, F5, F4, and F2 in descending order.

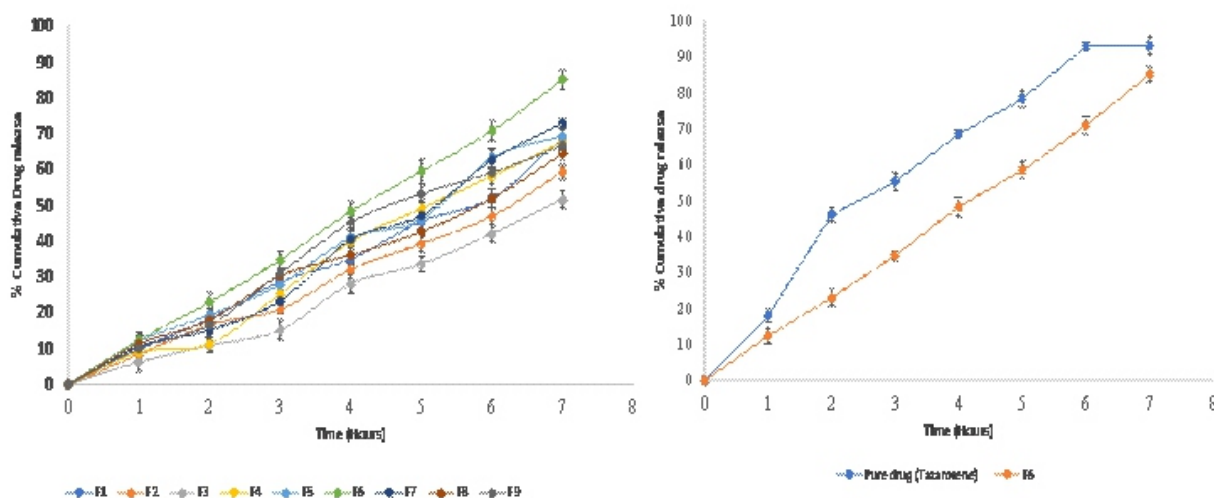


Figure 4: Drug release of emulgel formulations F1-F9 and optimized formulation F1 to plain drug solution

Ex vivo: Zone of Inhibition

Ex vivo studies evaluated the antibacterial activity of Tazarotene, a common acne medication, against *P. acnes* bacteria. Results showed that Tazarotene in an aqueous solution had a zone of inhibition of 29mm, indicating its antibacterial efficacy. An emulgel formulation containing Tazarotene had a slightly larger zone of inhibition of 30mm,

highlighting its enhanced antibacterial effectiveness. Conversely, an emulgel formulation with cinnamon oil but without Tazarotene had a reduced zone of inhibition of 9mm, and an emulgel formulation without Tazarotene or cinnamon oil had no zone of inhibition. These findings demonstrate the antibacterial potential of Tazarotene and its ability to improve the effectiveness of emulgel formulations.

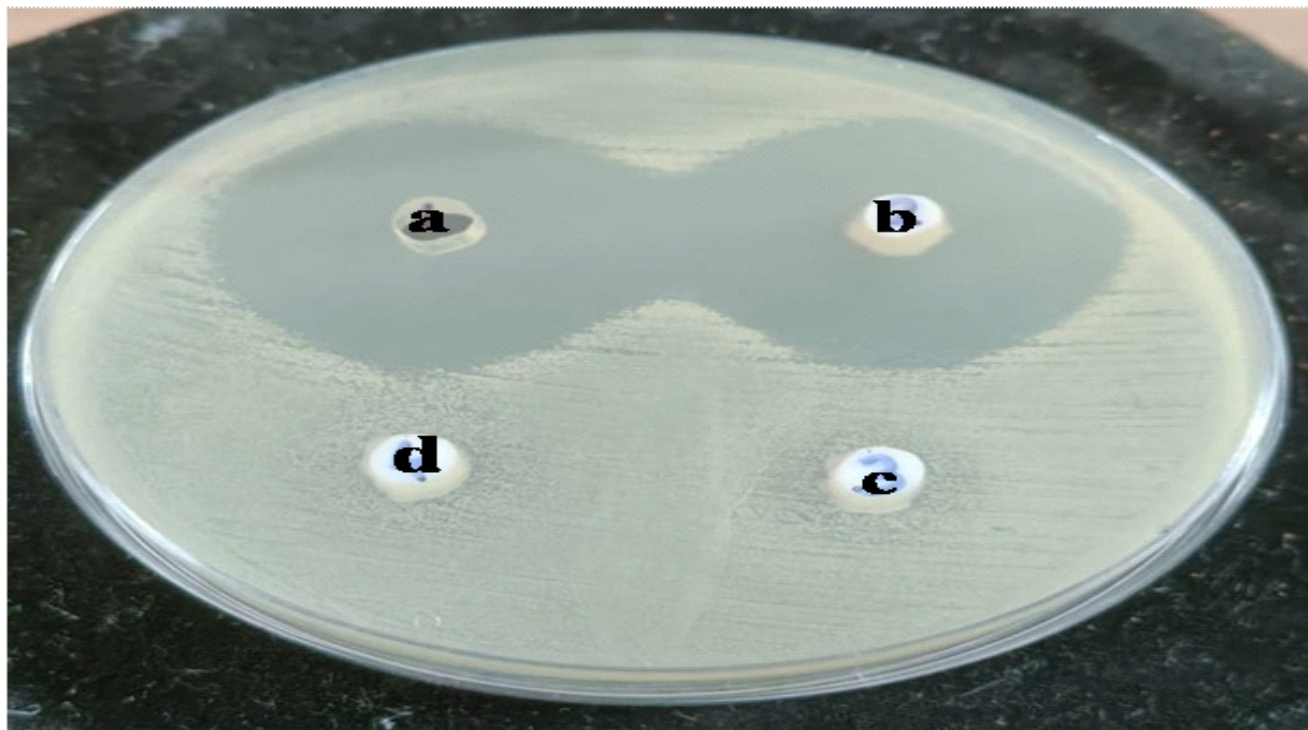


Figure 5:Zone of inhibition; a)plain tazarotene solution, b) the optimized emulgel formulation F6, c) emulgel formulation without the drug and cinnamon oil, d) an emulgel formulation without the drug

Ex vivo studies also identified the optimal formulation for antibacterial activity. The primary objective was to assess the antibacterial efficacy of Tazarotene against *P. acnes* bacteria. The well/disc diffusion method was used to evaluate various formulations, including a plain Tazarotene solution and different emulgel formulations. The emulgel formulation, exhibited the largest zone of inhibition against *P. acnes*, making it the preferred choice for subsequent investigations. These comprehensive studies confirmed the antibacterial potential of Tazarotene against *P. acnes* and identified Formulation as the most promising option for future research.

Discussion

The study was motivated by the prevalence of acne among adolescents, leading to the exploration of tazarotene, a retinoid known for its relevance in acne treatment and potential antibacterial properties against *P. acnes*. The objective was to address limitations in existing dermatological products by developing an emulsion-based emulgel that efficiently delivers both hydrophilic and hydrophobic drugs. Assessing formulations F1 to F9 across various parameters—pH, viscosity, spreadability, extrudability, swelling index, and drug content—highlighted Formulation F6 as the most promising option due to its balanced viscosity and pH, essential for effective emulgel creation. Optical microscopy confirmed successful oil droplet incorporation into the gel base, a key aspect for uniform drug distribution.

F6 exhibited superior spreadability and extrudability, crucial for ease of application, as well as higher drug content, release,

and enhanced antibacterial activity against *P. acnes* compared to other formulations. Swelling index measurements indicated varying water absorption, essential for emulgel properties. Collectively, these analyses underscore F6's potential as the most promising formulation for future development as an effective emulgel for acne treatment. Its high drug content and increased release of Tazarotene reinforce its potential for improved antibacterial efficacy against *P. acnes*. The comprehensive findings support Formulation F6's suitability for further investigation and development as an effective emulgel for acne treatment.

Conclusion

In conclusion, the research study was driven by the prevalence of acne, a common skin issue among adolescents, leading to the selection of tazarotene due to its relevance in acne treatment and potential antibacterial properties against *P. acnes*. The aim was to address the limitations of existing topical dermatological products by developing an emulsion-based emulgel capable of efficiently delivering both hydrophilic and hydrophobic drugs. Through the evaluation of various parameters including pH, viscosity, spreadability, extrudability, swelling index, drug content, in vitro drug release, and antibacterial activity, Formulation F6 emerged as the most promising choice. F6 exhibited optimal characteristics such as moderate viscosity and suitable pH, ensuring ease of application and absorption. Optical microscopy confirmed the successful incorporation of oil droplets into the gel base, essential for stable emulsion within the gel. Additionally, F6 demonstrated superior spreadability

and excellent extrudability, both crucial for effective topical application. Further, it showcased the highest drug content and a significantly higher release of Tazarotene, emphasizing its potential for enhanced antibacterial effectiveness against *P. acnes*. This comprehensive analysis supports the suitability of Formulation F6 for further investigation and development as an effective emulgel for acne treatment.

Acknowledgments

The author would like to acknowledge Glenmark Pharmaceuticals for providing Tazarotene (TAZ) as a gift sample, All India Council for Technical Education (AICTE), GPAT Fellowship, New Delhi.

References

- Ahmad, A., Tausif, M., Biswas, N. and Aftab, M., Study of Drug Utilization Pattern for Acne Vulgaris In The Department Of Dermatology At Integral Institute Of Medical Sciences And Research, Eur. Chem. Bull. 2023, 12 (S3), 6279 – 6289.
- Mias, C., Mengeaud, V., Bessou-Touya, S. and Duplan, H., 2023. Recent advances in understanding inflammatory acne: Deciphering the relationship between Cutibacterium acnes and Th17 inflammatory pathway. *Journal of the European Academy of Dermatology and Venereology*, 37, pp.3-11.
- Pawar, R. and Dawre, S., 2023. Solid lipid nanoparticles dispersed topical hydrogel for Co-delivery of adapalene and minocycline for acne treatment. *Journal of Drug Delivery Science and Technology*, 80, p.104149.
- Arooj, A., Rehman, A.U., Iqbal, M., Naz, I., Alhodaib, A. and Ahmed, N., 2023. Development of Adapalene Loaded Liposome Based Gel for Acne. *Gels*, 9(2), p.135.
- Garg, T., 2016. Current nanotechnological approaches for an effective delivery of bio-active drug molecules in the treatment of acne. *Artificial cells, nanomedicine, and biotechnology*, 44(1), pp.98-105.
- Common, J.E.A., Barker, J.N. and van Steensel, M.A., 2019. What does acne genetics teach us about disease pathogenesis?. *British Journal of Dermatology*, 181(4), pp.665-676.
- Xiang, Y., Lu, J., Mao, C., Zhu, Y., Wang, C., Wu, J., Liu, X., Wu, S., Kwan, K.Y., Cheung, K.M. and Yeung, K.W., 2023. Ultrasound-triggered interfacial engineering-based microneedle for bacterial infection acne treatment. *Science Advances*, 9(10), p.eadf0854.
- Badawi, N.M., Yehia, R.M., Lamie, C., Abdelrahman, K.A., Attia, D.A. and Helal, D.A., 2023. Tackling acne vulgaris by fabrication of tazarotene-loaded essential oil-based microemulsion: In vitro and in vivo evaluation. *International Journal of Pharmaceutics*, X, p.100185.
- Parmar, M.P., Paterl, L.D., Hadia, B.G., Rathod, L. and Parikh, K., 2019. Lipid based nanocarriers of Tazarotene for the treatment of Psoriasis: Optimization and In Vitro Studies. *World J. Pharm. Res*, 8, pp.1830-1871.
- Chodankar, D.S., Kudchadkar, S.S., Gude, R.S., Navti, P.D. and Sawant, S.M., 2020. Formulation Optimization And Evaluation Of Flurbiprofen Emulgel. *Int J Pharm Pharm Sci*.
- Goyani, M., Akbari, B., Chaudhari, S. and Jivawala, R., 2018. Formulation and evaluation of topical emulgel of antiacne agent. *International Journal of Advanced Research and Review*, 3(7), pp.52-68.
- Olayemi, O.J. and David, C., 2023. Emulgel: A Promising Technology for Topical Delivery of Herbal Extracts. *British Journal of Pharmacy*, 8(1).
- Baibhav, J., Gurpreet, S., Rana, A.C. and Seema, S., 2012. Development and characterization of clarithromycin emulgel for topical delivery. *Int J Drug Dev Res*, 4(3), pp.310-323.
- Charde, Y.M., Sharma, P.H., Choudhary, N.G. and Avari, J.G., 2014. Development and evaluation of herbal formulation for the treatment of acne. *International Journal of Pharmaceutical Sciences and Research*, 5(6), p.2250.
- Ambala, R. and Vemula, S.K., 2015. Formulation and characterization of ketoprofen emulgels. *Journal of Applied Pharmaceutical Science*, 5(7), pp.112-117.
- Bornare, P., More, R., Kute, P. and Bornare, P., 2023. HERBAL REMEDIES USED FOR THE TREATMENT OF ACNE VULGARIS.
- KhuntDM, Mishra AD, Shah DR. Formulation design & development of piroxicam emulgel. *Int J PharmTech Res*. 2012;4(3):1332-44.