RESEARCH ARTICLE

Development and Evaluation of Herbal Antiacne Gel Formulation Using Curcumin Phytosomes

Angum MM Ibrahim[1*], Siham K AbdelRahim[2], Huriyyah A Alturaifi[2], Intisar AM Elalawy[1]

[1]*Al Rayan Private College of Health Sciences and Nursing, Al Madinah Al Munawarah, , Saudi Arabia.*
[2]*Department of Chemistry, College of Science, King Khalid University, Abha, Saudia Arabia.*

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ABSTRACT

Acne vulgaris is a persistent inflammatory condition affecting the pilosebaceous unit that manifests as various skin lesions, including papules, comedones, cysts, pustules, and abscesses. Curcumin, extracted from *Curcuma longa* rhizomes (Family: Zingiberaceae), is identified for its potent antioxidant, wound-healing, and anti-inflammatory properties. This study aimed to develop an herbal antiacne gel formulation incorporating bioactive curcumin in phytosomes. The formulated gel was evaluated for several physicochemical properties, including pH, spreadability, viscosity, drug content, etc. Additionally, the optimized gel formulation was tested for its *in-vitro* antiacne action against *Propionibacterium acnes*. Results showed that developed antiacne gel containing curcumin phytosomes was comparable to a commercially available antiacne product. Stability studies demonstrated that the formulated product remained stable for three months under accelerated stability conditions as per ICH guidelines.

Keywords: Antiacne, Curcumin, Phytosomes, Antioxidant activity, gel.

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INTRODUCTION

Acne vulgaris is a persistent inflammatory condition affecting the pilosebaceous unit, most prevalent during adolescence, a time of significant psychosocial changes. This multifactorial disorder can manifest at any age but is most common between the ages of 12 and 24, affecting an estimated 85% of the population. An improved understanding of acne's pathophysiology has led to more rational and effective treatment approaches. The lesions of acne vulgaris are categorized into three categories: scars, inflamed lesions, and noninflamed lesions. Typical acne lesions embrace pustules, inflammatory papules, and comedones, while more critical cases may involve cysts and nodules, potentially leading to psychological distress and scarring.[1,2]

Acne arises when the sebaceous glands, which are connected to hair follicles, are activated during puberty due to increased amounts of androgens. Sebum, an inherent material that moisturizes and shields the skin, is generated in larger amounts, resulting in alterations in the maturation of skin cells that make hair follicles more prone to blockage. As the obstructed hair follicle increases in size, it creates a raised area. If the wall of the follicle breaks, substances that cause irritation and germs that naturally reside on the skin can enter deeper layers of the skin, leading to inflammation.[3]

While synthetic drugs are commonly used to treat acne, they may cause significant side effects, and prolonged use can lead to resistance in acne-causing bacteria. Minerals and natural products derived from animals and plants have the potential to treat numerous human diseases, and herbal medicine is gaining popularity due to the toxicity and side effects related to manmade medicines.[4]

Turmeric, derived from the rhizomes of *Curcuma longa* (family: Zingiberaceae), includes curcuminoids, which are a mixture of curcumin (diferuloylmethane), demethoxycurcumin, and bis-demethoxycurcumin. Curcumin, the primary active component, constitutes about 90% of the curcuminoid content in turmeric. Research has demonstrated that curcumin has strong anti-inflammatory, wound-healing, and antioxidant properties, making it potentially therapeutic against acne. Turmeric is considered safe when consumed in dietary amounts or applied topically in medicinal quantities. Curcumin has been found to offer therapeutic promise for disorders such as chronic anterior uveitis, arthritis, pancreatitis, inflammatory bowel disease, and certain forms of cancer, according to clinical research.[5,6]

Mild acne is commonly treated with benzoyl peroxide, azelaic acid, and topical retinoids (tretinoin and adapalene). For moderate acne, treatment options include topical antibiotics

**Author for Correspondence: anjumibrahem@gmail.com*

like clindamycin and erythromycin, oral antibiotics like erythromycin and tetracycline, isotretinoin, and hormonal therapies such as estrogen and estrogen-containing oral contraceptives. Severe acne is often treated with isotretinoin. However, synthetic drugs can cause side effects like mild irritation, dryness, contact dermatitis, nausea, diarrhea, sore eyes, itchy skin, and bacterial resistance, particularly from antibiotics.[7]

Plant-based natural medicines are gaining popularity over synthetic pharmaceuticals due to their numerous benefits, such as less side effects, improved patient tolerance, lower expenses, and a well-established historical usage.[8] Phytosomes have been discovered to enhance the solubility, permeability rate, and bioavailability of active chemicals in different scenarios. They also prevent or postpone physical and chemical degradation and can be used without causing any adverse consequences. The empirical of the current research was to develop and assess an herbal topical gel using phytosomes of curcumin for acne treatment that is as effective as marketed formulations.

MATERIALS AND METHODS

Materials

The curcumin compound, with a purity level of 97%, was acquired from High Purity Chemicals Private Limited, located in Mumbai, India. Soybean phospholipids (lipoid P75 and Phospholipon 90 H) were acquired as a free sample from Lipoid. We obtained non-genetically modified soybean phospholipid (IP) from Happy Food Company in India. All reagents utilized in the investigation were of analytical reagent grade.

Preformulation studies

Identification of curcumin and preparation of its calibration curve

A standard curve for curcumin was generated by preparing a series of curcumin solutions with concentrations ranging from 2 to 14 µg/mL. The standard solution (10 µg/mL) was scanned over a wavelength range of 200 to 800 nm. The solutions were analyzed for absorbance at a wavelength of 420 nm using a UV-visible spectrophotometer (Make: Shimadzu) equipped with two matched quartz cells of 1 cm path length. The calibration curve was drew by graphing concentration against absorbance, and the correlation coefficient was calculated.

Compatibility Study

FTIR spectroscopy

Compatibility studies were conducted to identify potential chemical interactions between curcumin and the excipients utilized in the formulation. A physical mixture of the medication and all excipients was prepared for this purpose. Compatibility between excipients and medication was assessed using FTIR spectroscopy. FTIR spectra were logged between 400 to 4000 cm^{-1} with an FTIR Spectrophotometer (Make: Shimadzu).

Differential scanning calorimetry (DSC)

In order to conduct a more thorough examination of possible interactions between drugs and excipients, an investigation using differential scanning calorimetry (DSC) was performed. The analysis employed a Mettler Toledo 821e Differential Scanning Calorimetry device manufactured by Mettler Toledo in Switzerland. In the investigation, a quantity of 10 mg from every sample was retained in an aluminum pan and exposed to heating at 10°C per minute. The temperature range covered was from 30 to 305°C, and a nitrogen flow of 10 ml per minute was maintained throughout the process. Alumina served as the reference standard.

Formulation Development

Preparation of curcumin phytosomes

The curcumin and soy phospholipid were precisely measured and mixed in 20 mL of pure alcohol in a round bottom flask with 100 mL capacity. The resulting mixture was agitated at a temperature of 5°C for a duration of 35 minutes using a rotary evaporator operating at a speed of 90 rpm. The thin film on an inner surface of the RBF was moistened with 10 mL of distilled H_2O. Suspension containing H_2O molecules was subjected to ultrasonic vibrations for a duration of 10 minutes using a Probe sonicator. Next, the resulting dispersion was centrifuged at 15000 revolutions per minute for a duration of 30 minutes. The liquid portion was discarded and the phytosomes that had settled were dried in an oven at 45°C for a duration of 12 hours. The dehydrated phytosomal substance was further filtered using a 100-mesh sieve to acquire a fine phytosomal powder. The displaced powder was kept in a cool location within a hermetically sealed container until it is needed again.[7-10]

Preparation of antiacne gel

Propyl and methylparaben were first dissolved in distilled H_2O before incorporating a gelling agent. To prepare carbopol gel, Carbopol 940 was soaked in water and then neutralized with triethanolamine to bring the pH to a level suitable for normal skin. After adjusting the pH, a weighed quantity of curcumin phytosomes was added to the final carbopol gel base.[1-5] Table 1 provides a composition of the optimized curcumin phytosomal antiacne gel formulation.[11-12]

Evaluation of antiacne herbal gel

The quality of the formulated gel was evaluated using the following parameters:

Table 1: Composition of antiacne herbal gel

Ingredients	*Quantity (g)*
Curcumin phytosomes equivalent to pure curcumin	0.1
Carbopol 940	0.02
Triethanolamine	q. s. to adjust pH to neutral
Methylparaben	0.02
Propylparaben	0.01
Water	q. s. to 10

q.s.: Quantity sufficient

Physical evaluation

The gel's color and appearance were assessed visually against contrasting backgrounds.[13]

Measurement of pH

pH of this gel was verified utilizing a digital pH meter, standardized with typical buffer solutions at pH 7 and 4. To perform the measurement, 1 g of the gel formulation was dissolved in approximately 10 mL of distilled H_2O, stirred to form a uniform dispersion, and allowed to sit for 2 hours. This solution was then diluted to 100 mL, and the pH was measured using calibrated pH meter.[14]

Spreadability

Spreadability was assessed using an apparatus consisting of a wooden block with a pulley at one end. This method quantifies the extent to which a gel can spread by evaluating its slip and drag characteristics. Approximately 2 g of the gel was applied onto a stationary ground slide. Ground slide was then placed linking an added glass slide that had a hook matching the size of the slide. A 100 g weight was applied for a duration of 5 min to eject air and establish a consistent film. Surplus gel was removed from the margins. The upper slide was subsequently dragged by a 50 g weight utilizing a string fastened to a hook, and the duration needed for the upper slide to traverse to 30 cm was documented. Spreadability is determined by a shorter duration, which is computed utilizing the below given equation:

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

Here
S = Spreadability
M = Weight in pan (attached to upper slide)
L = Distance moved by glass slide
T = Duration required for the slides to fully detach from one another (in sec).

Viscosity

The viscosity of the gel was assessed utilizing a Brookfield viscometer with spindle No. 6 at 10 rpm for 2 minutes at room temperature.

Determination of medication content

The medication content of optimized antiacne gel was assessed using a previously validated UV spectroscopic method. Approximately 100 mg of this gel was dissolved in 10 mL of ethanol by sonication to get a solution with a 10,000 µg/mL concentration. This stock solution was sufficiently diluted to a final concentration of about 5 µg/mL. The absorbance of this solution was measured, and the drug content was calculated using a calibration curve constructed in ethanol.[15]

Antioxidant study

The antioxidant activity of this gel was assessed utilizing H_2O_2 free radical scavenging method, as reported in prior literature. The gel's ability to scavenge hydrogen peroxide was assessed by preparing a 25 mmol/l solution of H_2O_2 in phosphate buffer (pH 7.4). Diluted formulations (1–5% v/v) were added to 0.6 mL H_2O_2 solution, and absorbance was assessed at 230 nm after 10 minutes against a blank phosphate buffer solution without H_2O_2. A separate blank was employed for each concentration.[16-18] %scavenging activity was determined utilizing below given equation:

$$\%Scavenging\ Activity = \frac{[Absorbance\ of\ Control - Absorbance\ of\ Sample]}{Absorbance\ of\ Control}\ X\ 100$$

Antiacne study

The antibacterial activity of this gel was estimated utilizing the broth dilution method, a traditional *in-vitro* test for bacterial susceptibility. This method provides a quantitative result for the concentration of antimicrobial agents required to inhibit specific microorganisms. The test was conducted in tubes following procedures detailed in previous literature. The gel sample was prepared in two-fold dilutions (5, 25, 50, 100, 250, and 500 µg/mL) in a liquid growth medium, with DMSO (dimethyl sulfoxide) as the diluent. A standardized bacterial suspension (1–5×10^5 CFU/mL) was utilized to inoculate test tubes. Following an overnight incubation at a temperature of 37°C, tubes were inspected for the presence of visible bacterial growth, which was identified by the presence of turbidity. The gel sample's minimal inhibitory concentration (MIC) was determined as the lowest concentration that hindered growth. [19]

Stability study

A stability study was conducted according to ICH recommendations. The prepared gel was placed in wide-mouth glass containers and kept at 40 ± 2°C with 75% ± 5% RH for 3 months. The gel was periodically assessed for appearance, drug content and pH.[20]

RESULTS AND DISCUSSION

Pre-formulation Studies

Identification of curcumin and preparation of its calibration curve

The maximum absorbance wavelength (λ max) of curcumin was found to be 425 nm, which closely aligns with the reported literature value. This consistency confirms the identity of the curcumin utilized in this study.[21] UV spectrum of curcumin is shown in Figure 1.

A calibration curve was built by drawing the various concentrations of curcumin against their corresponding mean absorbance values. The calibration curve is illustrated in Figure 2. From this data, the slope, intercept, correlation coefficient (R^2), and regression equation were derived. The resulting linear equation was y = 0.1645x +0.0821, where x represents concentration and y represents absorbance. The correlation coefficient of 0.9984 implies a strong linear association within the selected concentration range.

Compatibility Studies

By FTIR spectroscopy

The FTIR spectrum of curcumin exhibited a distinctive O-H stretching band at 3512 cm^{-1}. The peak at 2922 cm^{-1} corresponded to C-H stretching, while the peak at 1602 cm^{-1}

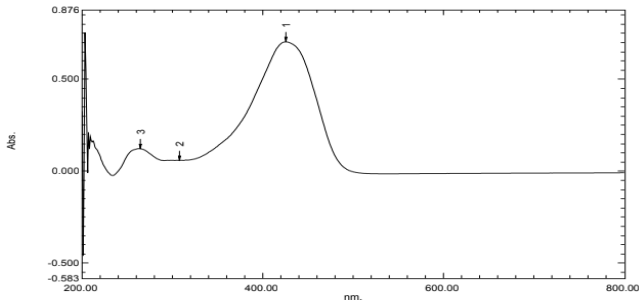

Figure 1: UV- Spectrum of curcumin

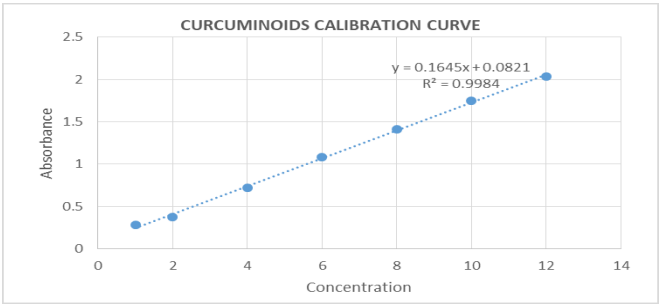

Figure 2: Calibration curve of standard curcumin

was associated with C=C symmetric stretching in the aromatic ring. The peak at 1510 cm^{-1} indicated C=O stretching, and enol C-O stretch was observed at 1280 cm^{-1}. Additionally, the benzoate trans-C-H vibration appeared at 962 cm^{-1}. These spectral features are consistent with those reported in the literature.[1]

The FTIR spectrum of the physical mixture showed peaks that align with those observed in the curcumin spectrum, with no new or well-defined interactions between curcumin and the excipients. It suggests curcumin is consistent with other constituents of formulation. The FTIR spectra for both the pure medication and the physical mixture are presented in Figures 3 and 4, respectively.

Differential scanning calorimetry (DSC)

The DSC thermogram of curcumin displayed a sharp endothermic peak at 180°C, which is close to the melting point of pure curcumin reported as 183°C. DSC analysis indicated that the melting point of pure curcumin is 180°C, while in the formulation, it is 176.2°C. The minor shift in the melting point observed in the formulation thermogram suggests that the drug remains in a largely pure state without significant interaction with the excipients. The slight decrease in melting point is attributed to the effect of the excipients. Figures 5 and 6 show the DSC thermograms for pure curcumin and the optimized gel formulation, respectively.

Formulation Studies

Formulation development

Excipients were chosen based on information from previous literature. Their concentrations were optimized through trial and error. Curcumin was selected for its potent antioxidant, wound healing, and anti-inflammatory properties. This

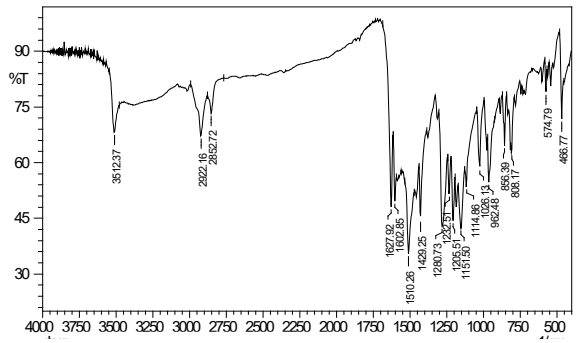

Figure 3: FTIR of pure curcumin

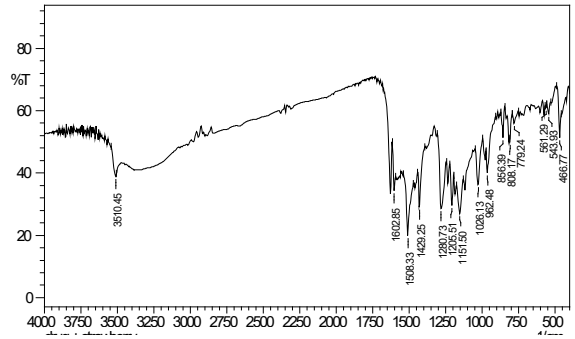

Figure 4: FTIR of physical mixture

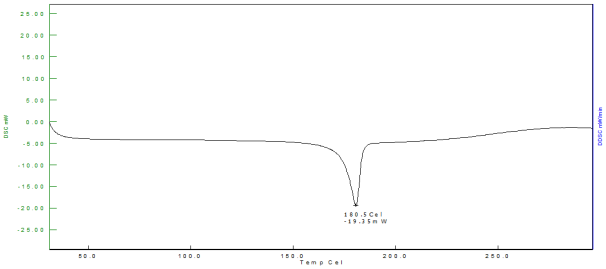

Figure 5: Differential scanning calorimetry of pure curcumin

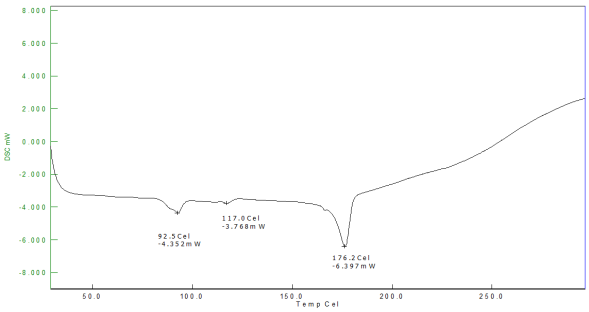

Figure 6: DSC of developed gel formulation

ingredient thus was chosen for the antiacne gel formulation. Carbopol 940 served as the gelling agent, while triethanolamine was used to adjust the pH. Methyl paraben and propyl paraben were included as preservatives.

Evaluation of gel formulation

Results of the evaluation of the prepared herbal antiacne gel are briefed in Table 2.

Table 2: Evaluation results of formulated gel

Parameters	*Results*
Appearance	Yellow
Spreadability	80 g cm/sec
Viscosity	50,000 cps
pH	6.9
Drug content (Assay)	99.58% w/w

The pH of the gel was approximately neutral, suggesting that the formulation is unlikely to cause skin irritation upon topical application. The gel's viscosity, measured at 50,000 cps, provides the desired consistency to prevent it from flowing off the skin. Additionally, a spreadability value of 80 g cm/sec ensures that the gel forms a uniform layer when applied.

Antioxidant study

The antioxidant activity of ascorbic acid and herbal antiacne gel was evaluated using the H_2O_2 assay method. The results are presented in Table 3 for ascorbic acid and Table 4 for the herbal antiacne gel.

The results suggest that the test compounds effectively eliminated free radicals in a manner that was influenced by the dosage. Standard ascorbic acid demonstrated a 96.12% scavenging activity at a concentration of 10 µg/mL, with an IC_{50} value of 3.31 µg/mL. In comparison, herbal antiacne gel exhibited a percent scavenging activity of 97.11% and a lower IC_{50} value of 2.21 µg/mL. This suggests that the developed antiacne gel has superior free radical scavenging activity associated with ascorbic acid. Figures 7 and 8 illustrate the free radical scavenging activity of ascorbic acid and herbal antiacne gel, respectively.

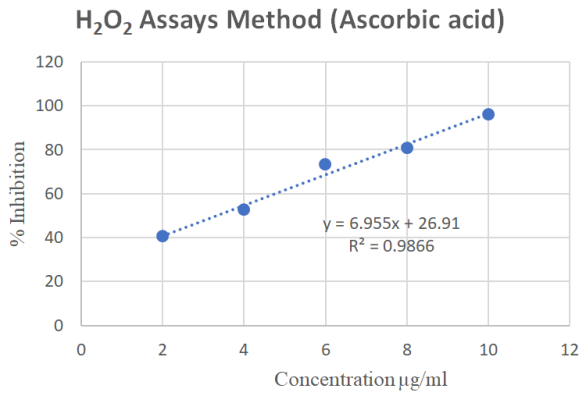

Figure 7: Graphical representation of %inhibition of free radicals by H_2O_2 assays method (Ascorbic acid)

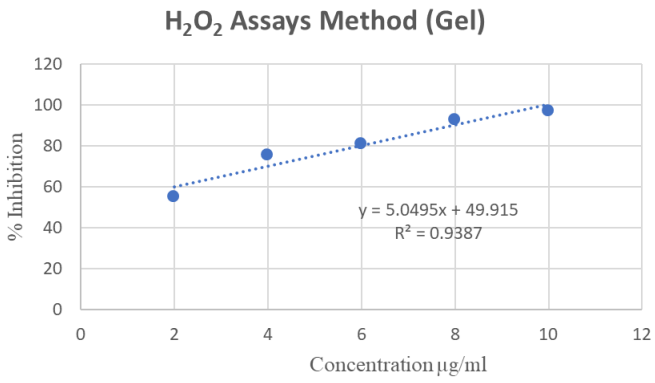

Figure 8: Antioxidant activity of herbal antiacne gel by H_2O_2 assay method

Table 3: Percent inhibition of free radicals by H_2O_2 assay method (Ascorbic acid)

Concentration (µg/mL)	*%Inhibition*
2	40.55
4	52.78
6	73.01
8	80.74
10	96.12

Table 4: Percent inhibition of free radicals by H_2O_2 assay method (Herbal antiacne gel)

Concentration(µg/ml)	*% Inhibition*
2	66.23
4	75.34
6	80.81
8	92.57
10	97.11

Table 5: Comparative study of antiacne activity of herbal antiacne gel and marketed gel on *Propionibacterium acnes*

S. No.	*Sample*	*Zone of inhibition (mm)*					
		P. acnes (MTCC 1951) Concentration in µg/ml					
		5	*25*	*50*	*100*	*250*	*500*
1	Curcumin phytosomal gel	-	11	13	17	19	25
2	Marketed gel (standard)	-	12	15	19	20	27

Antiacne study

The results of the antiacne activity of herbal antiacne gel and marketed antiacne gel formulation are depicted in Table 5.

The results demonstrate that the antiacne activity of herbal antiacne gel is comparable to that of a synthetic marketed antiacne gel. The zone of inhibition for the herbal antiacne gel was 21 mm, while the synthetic gel exhibited a 23 mm zone of inhibition. This suggests that the formulated antiacne gel is effective in treating acne vulgaris. Additionally, the herbal nature of the gel provides a safer alternative compared to synthetic products. The active phytoconstituent in the herbal antiacne gel is curcumin (diferuloylmethane), a flavonoid curcuminoid known for its potent antioxidant, wound-healing, and anti-inflammatory properties, which contribute to its therapeutic efficacy against acne.

Table 6: Results of stability study

Parameter	*Initial*	*Month-1*	*Month-2*	*Month-3*
Physical Appearance	Yellow color	Unchanged	Unchanged	Unchanged
pH	6.91	6.93	6.89	6.88
Drug content (% w/w)	99.58	99.40	98.87	98.55

Stability studies

The results of the stability study of antiacne gel are briefed in Table 6.

According to the ICH criteria, the stability investigations showed that the created formulation remains stable for a period of three months under accelerated stability circumstances.

CONCLUSION

Development and evaluation of the curcumin phytosome-based antiacne gel have demonstrated promising results across various parameters. The formulation prepared utilizing curcumin phytosomes has shown effective antioxidant and antibacterial properties, crucial for its intended use as an antiacne treatment. The gel's pH, viscosity, and spreadability were optimized to ensure skin compatibility and effective application.

The antioxidant activity of the gel was found to be comparable to, if not exceeding, that of standard ascorbic acid, indicating its potent ability to scavenge free radicals. The antiacne efficacy was also notable, with the herbal antiacne gel exhibiting an inhibition zone similar to that of a synthetic antiacne gel, thus confirming its therapeutic potential.

Additionally, the formulation's stability and lack of significant drug-excipient interactions further support its potential for safe and effective use. Overall, the developed curcumin-based gel represents a viable herbal alternative to synthetic antiacne treatments, benefiting from curcumin's known therapeutic properties.

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