**RESEARCH ARTICLE**

# Development and Evaluation of a Topical Gel Containing 0.1% Adapalene and 2.5% Benzoyl Peroxide for Acne Treatment

Ngan-Hanh-Thao Nguyen[1], Dang-Khoa Nguyen[2], Phu-Gia Tran[3], Le-Duy Ly[3], Minh-Tri Le[3], Minh-Quan Le[4], Van-Ha Nguyen[4*]

[1]*Faculty of Pharmacy, Nguyen Tat Thanh University, Ho Chi Minh City 700000, Vietnam*
[2]*Faculty of Pharmacy, Ton Duc Thang University, Ho Chi Minh City 700000, Vietnam*
[3]*University of Health Sciences, Vietnam National University, Ho Chi Minh city 700000, Vietnam*
[4]*Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh city, Ho Chi Minh 700000, Vietnam*

***Received: 11th Apr, 2025; Revised: 10th Jun, 2025; Accepted: 15th Jun, 2025; Available Online: 25th Jun, 2025***

**ABSTRACT**

The gel product that combines two active ingredients adapalene (AD) and benzoyl peroxide (BO) has been used for a long time with good acne effectiveness and is licensed in the treatment of moderate to severe acne. On the market today, there are a few acne products containing these two active ingredients, however, the formula and preparation process have not been announced. Therefore, the study was conducted to research and prepare a gel product that combines AD 0.1% and BO 2.5%. The study results show that the gel formulation uses excipients Simugel SMS88 (6%), propylene glycol (4%), glycerin (4%), sodium docusate (0.05%), poloxamer 188 (0.2%). ) and demineralized water (83.15%) for a soft, pleasant physical sensation when applied, equivalent to a famous product (named X, which has the same ingredients and contents) in terms of parameters such as thinness, release of active ingredients, *in vitro* permeability . The results of stability monitoring under accelerated conditions for 6 months showed that the gel product had no significant physical or chemical changes. The research has successfully built the formula and process of preparing a gel product that combines the two active ingredients. The research results can be applied in upgrading larger batch sizes and deployed in production in the future.

**Keywords:** Adapalen, benzoyl peroxid, gel, simugel sms88, *in vitro* release, *in vitro* permeability

**How to cite this article:** Ngan-Hanh-Thao Nguyen, Dang-Khoa Nguyen, Phu-Gia Tran, Le-Duy Ly, Minh-Tri Le, Minh-Quan Le, Van-Ha Nguyen. Development and Evaluation of a Topical Gel Containing 0.1% Adapalene and 2.5% Benzoyl Peroxide for Acne Treatment. International Journal of Drug Delivery Technology. 2025;15(2):391-96. doi: 10.25258/ijddt.15.2.3

**Source of support:** This research was funded by the Vietnam National University – Ho Chi Minh City (VNU-HCM) under project code C2020-44-04.

**Conflict of interest:** None

## INTRODUCTION

Adapalene (AD) is a derivative of naphthoic acid that was approved by the FDA in 1996 for the treatment of acne vulgaris in patients over 12 years of age. AD is considered a first-line treatment for acne and is available in various topical dosage forms such as gels, creams, and lotions.[1] Benzoyl peroxide (BO), a chlorohydroxyquinoline derivative, has been widely used in the treatment of moderate to severe acne, either as monotherapy or in combination with certain antibiotics and oral retinoids.[2] Acne vulgaris (AV) is a prevalent dermatological condition characterized by symptoms such as pain, itching, and erythema.[3] In acne treatment regimens, topical formulations are prioritized due to their ability to minimize systemic toxicity and side effects associated with oral therapies.[4] Among these, gel formulations offer significant advantages due to their non-greasy texture and ease of removal. In particular, hydrophilic gels are known for their rapid drug release, high uniformity, and good stability.[5] Common active ingredients used in acne treatment include tretinoin, BO, antibiotics, and various anti-inflammatory agents.[6] Compared to monotherapy, combination products containing multiple active ingredients have demonstrated superior clinical efficacy. The combination of an antimicrobial agent and a topical retinoid in a single formulation is currently one of the most recommended approaches.[7] A combination of adapalene 0.1% and benzoyl peroxide 2.5% has been approved for the treatment of moderate to severe acne in patients aged 12 years and older. This combination therapy has shown greater efficacy than monotherapy with either adapalene 0.1% or benzoyl peroxide 2.5% alone.[8] Currently, commercial gel products containing both AD and BO include Epiduo® and Tactuo®. However, the formulation composition and preparation process of these products have not been disclosed. Therefore, this study aims to develop a gel formulation and manufacturing process for a product containing adapalene 0.1% and benzoyl peroxide 2.5%, and to compare it with a well-known reference product containing the same active ingredients at equivalent concentrations.

## MATERIALS AND METHODS

**Author for Correspondence: nguyenvanha@ump.edu.vn*

Table 1: The criteria of Product X

| No. | Criteria | Results | |
|---|---|---|---|
| 1 | Appearance | Opaque white, soft and smooth texture, non-greasy, non-sticky when applied to skin, easily spreadable. | |
| 2 | pH | 5.04 ± 0.1 | |
| 3 | Homogeneity | No visible particles in 4 tested samples. | |
| 4 | Viscosity (cps) | 408389 ± 20 | |
| 5 | Spreadability (cm) | 4.61 ± 0.05 | |
| 6 | Content (%) | AD: 100.77 | BO: 104.78 |
| 7 | Drug release (%) | AD: 99.17 | BO: 100.58 |

*Materials*

Chemicals and Excipients: Acetonitrile (Merck, Germany), Tetrahydrofuran (Merck, Germany), Trifluoroacetic acid (Merck, Germany), HPLC-grade distilled water (Vietnam), Adapalene, Benzoyl peroxide (Xilong Scientific, China), Reference product X (France), Glycerin (China), Propylene glycol (Xilong Scientific, China), Carbopol 940, Sodium CMC, Sodium benzoate (Xilong Scientific, China), Ascorbic acid, Citric acid, Triethanolamine (Xilong Scientific, China), Adapalene reference standard (Sigma-Aldrich, USA), Benzoyl peroxide reference standard (Sigma-Aldrich, USA).

Instruments and Equipment: UV-Vis spectrophotometer Shimadzu UV-1800 (Shimadzu, Japan), HPLC system SHIMADZU (Japan), Overhead stirrer IKA RW (Germany), Magnetic stirrer with heating (VELP, Italy), pH meter (Mettler Toledo, Switzerland), Brookfield viscometer Model DV2TRV (Brookfield, USA), Heated shaking water bath (Stuart SBS40, USA), Analytical balance (KERN, Germany), Ultrasonic bath (Elmasonic S 60 H, KERN, Germany), Climatic chamber (Memmert, Germany).

*Methods*

*Evaluation of the Commercial Comparator Product X*

The appearance of the product was evaluated through visual observation to document its physical characteristics. Homogeneity was assessed in accordance with the standards specified in Appendix 1.12 "Topical and Mucosal Preparations" of the Vietnamese Pharmacopoeia V. Viscosity was measured using a Brookfield viscometer, with appropriate settings adjusted based on the sample's consistency. The pH was determined using a dual-electrode pH meter.

*In Vitro Drug Release Study*

The drug release was assessed by HPLC, based on the method developed by Van-Ha Nguyen, et al. (2020) for the simultaneous quantification of adapalene (AD) and benzoyl peroxide (BO) in gel formulations.[9] The solvent used was a mixture of tetrahydrofuran and acetonitrile (THF:ACN) in a 45:55 ratio. To perform the procedure, 1 g of gel was accurately weighed into a stoppered Erlenmeyer flask, followed by the addition of exactly 25 mL of the solvent. The mixture was stirred magnetically at 100 rpm for 2 hours. After stirring, the solution was collected, filtered through a 0.45 μm membrane, and the amount of drug released was quantified using HPLC. The percentage of drug released was calculated using the following formula:

Drug release (%) = $(C_t / C_{avg}) \times 100$

Where:

$C_t$: Concentration of the active ingredient in the solvent after 2 hours of stirring

$C_{avg}$: Average concentration of the active ingredient in the formulation

Table 2: Formulations investigating hydrophilic gel-forming excipients

| Formula-tion | Simulgel SMS 88 (%) | Sepineon (%) | NaCMC (%) | Carbomer (%) | TEA (%) | Purified water (%) | Spreadability (cm) | Viscosity (cps) | Appearance |
|---|---|---|---|---|---|---|---|---|---|
| F1 | 3 | - | - | - | - | 97 | 5.87± 0.05 | 325547± 24 | Poor |
| F2 | 4 | - | - | - | - | 96 | 5.3± 0.1 | 360559± 20 | Poor |
| F3 | 5 | - | - | - | - | 95 | 5.03± 0.04 | 379913± 16 | Poor |
| F4 | 6 | - | - | - | - | 94 | 4.67± 0.2 | 409200± 15 | Poor |
| F5 | - | 2 | - | - | - | 98 | 5.73± 0.1 | 333501± 35 | Poor |
| F6 | - | 2.5 | - | - | - | 97,5 | 4.93± 0.2 | 377619± 30 | Good: smooth, soft, and pleasant |
| F7 | - | 3 | - | - | - | 97 | 4.7± 0.15 | 376588± 24 | Poor |
| F8 | - | 4 | - | - | - | 96 | 4.63± 0.05 | 412735± 21 | Good: smooth, soft, and pleasant |
| F9 | - | - | 2 | - | - | 98 | 4.5± 0.13 | 424659± 17 | Good: smooth, soft, and pleasant |
| F10 | - | - | 3 | - | - | 97 | 4.1± 0.11 | 466088± 15 | Poor |
| F11 | - | - | 4 | - | - | 96 | 3.37± 0.08 | 567052± 22 | Poor |
| F12 | - | - | 5 | - | - | 95 | 3.1± 0.04 | 616440± 23 | Poor |
| F13 | - | - | - | 0.5 | 0.5 | 99 | 4.34± 0.12 | 440314± 18 | Good: smooth, soft, and pleasant |
| F14 | - | - | - | 1 | 1 | 98 | 4.67± 0.14 | 409200± 24 | Poor |
| F15 | - | - | - | 1.5 | 1,5 | 97 | 5.2± 0.07 | 367493± 16 | Poor |
| F16 | - | - | - | 2 | 2 | 96 | 5.63± 0.05 | 339425± 19 | Poor |

Table 3: Drug release profiles of Formulations F6, F8, F9, and F14

| Ingredients | F6 | | F8 | | F9 | | F14 | | Product X | |
|---|---|---|---|---|---|---|---|---|---|---|
| AD (%) | 0.1 | | 0.1 | | 0.1 | | 0.1 | | | |
| BO (%) | 2.5 | | 2.5 | | 2.5 | | 2.5 | | | |
| Simulgel SMS 88 (%) | 6 | | - | | - | | - | | | |
| Sepineon 600 (%) | - | | 4 | | - | | - | | | |
| NaCMC (%) | - | | - | | 2 | | - | | | |
| Carbomer 940 (%) | - | | - | | - | | 1 | | | |
| Triethanolamin (%) | - | | - | | - | | 1 | | | |
| Nước RO (%) | 91.4 | | 93.4 | | 95.4 | | 95.4 | | | |
| Drug release (%) | AD | BO | AD | BO | AD | BO | AD | BO | AD | BO |
| | 96.85 | 96.68 | 96.53 | 98.81 | 80.15 | 83.88 | - | - | 99.17 | 100.58 |
| pH | 6.45 ± 0.1 | | 5.3 ± 0.2 | | 6.15 ± 0.15 | | 7.21 ± 0.12 | | 5.04 ± 0.1 | |

Table 4: F6-based formulations with auxiliary excipients

| | | F6.1 | F6.2 | F6.3 | F6.4 | F6.5 | F6.6 |
|---|---|---|---|---|---|---|---|
| AD (%) | | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| BO (%) | | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| PG (%) | | 2 | 2 | 4 | 4 | 8 | 8 |
| G (%) | | 4 | 8 | 4 | 8 | 4 | 8 |
| Docusate sodium (%) | | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| Poloxamer 188 (%) | | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Simulgel SMS 88(%) | | 6 | 6 | 6 | 6 | 6 | 6 |
| Purified water | | qs to 100% | qs to 100% | qs to 100% | qs to 100% | qs to 100% | qs to 100% |
| Assay (%) | AD | 102.20 | 100.77 | 105.84 | 103.98 | 105.73 | 100.72 |
| | BO | 117.68 | 104.78 | 101.32 | 102.04 | 118.7 | 102.04 |

*In Vitro Permeation Study*

Accurately weigh 1 g of gel into a cellulose acetate dialysis bag, seal both ends, and immerse in exactly 25 mL of diffusion medium (DM) in a stoppered Erlenmeyer flask. The setup was incubated in a thermostatic shaking water bath. Samples were collected at 1, 2, 4, 6, and 7 hours, and the withdrawn volume was replaced with an equal volume of fresh DM. The test was conducted under the following parameters and conditions.[10,11] Stirring speed of 100 rpm, temperature maintained at 32 ± 0.5 °C, and a dialysis bag size of 7 × 3 cm. The sampling volume was 2 mL, and the diffusion medium consisted of a phosphate buffer (pH 7.4) and tetrahydrofuran (THF) mixed in a 50:50 (v/v) ratio.

The cumulative percentage of drug released was calculated using the following formula:

$X_t = (Q_t \times 100) / M$

Where:

$X_t$: Percentage of drug released at time t (%)

$Q_t$: Cumulative amount of drug released at time t (mg)

M: Average content of drug in 1 g of the formulation

*Formulation Development and Gel Preparation Process*

The gel formulation was developed for a batch size of 50 g. Appropriate quantities of gelling agents were accurately weighed and dispersed/swollen in a small amount of distilled water to form a semi-solid hydrogel base. Active ingredients were accurately weighed and dissolved/dispersed in suitable solvents before incorporation into the hydrogel under continuous stirring. Other excipients were gradually added to the mixture while stirring until uniform. The final gel mass was adjusted to 50 g using deionized water. The formulation was deaerated by storing in a refrigerator for 24 hours. Preliminary evaluations including organoleptic properties and pH were performed. The gels were stored at room temperature, protected from light.

Each prepared formula was evaluated for the following criteria: appearance, homogeneity, viscosity, pH, and in vitro permeability. Based on the evaluation results, the optimal formulation was selected and compared to the commercial product X. The selected formulation was scaled up to a batch size of 50 g and underwent finished product quality control for final formulation validation.

*Preliminary Stability Study*

The stability study was conducted under accelerated conditions at 40 ± 2 °C and 75% ± 5% relative humidity. Samples were collected at 0, 3, and 6 months for evaluation. A single batch was monitored throughout the study, and preliminary conclusions were drawn regarding the physical and chemical stability of the product under these storage conditions.

## RESULTS AND DISCUSSION

*Evaluation of the Criteria of the Reference Product X*

The criteria of the reference product X are presented in Table 1.

Product X has a soft and smooth texture, providing a pleasant skin feel, with a suitable pH for skin (slightly acidic or neutral [5]). The homogeneity (according to Vietnamese Pharmacopoeia V[12]) and the active ingredient content (according to USP 40[13,14]) meet pharmacopeial standards. The 2-hour drug release of adapalene (AD) and benzoyl peroxide (BO) from product X were 99.17% and 100.58%, respectively. As there is no specific standard for drug release from topical products, a proposed standard is that the release of both actives after 2 hours should be ≥ 95% of the labeled content.

*Formulation Development and Gel Preparation Process*

Table 5: Drug release (%) from F6-based supportive formulations

| Time | F6.1 | | F6.2 | | F6.3 | | F6.4 | | F6.5 | | F6.6 | | Product X | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (hour) | AD | BO | AD | BO | AD | BO | AD | BO | AD | BO | AD | BO | AD | BO |
| 1 | 4.66 | 1.43 | 1.83 | 1.25 | 9.37 | 4.76 | 7.71 | 3.17 | 7.44 | 3.93 | 3.24 | 1.36 | 6.68 | 2.60 |
| 2 | 7.33 | 1.92 | 2.45 | 1.63 | 14.28 | 5.84 | 10.84 | 3.89 | 9.03 | 4.56 | 6.92 | 1.80 | 9.85 | 3.37 |
| 4 | 8.98 | 2.83 | 3.57 | 2.34 | 33.02 | 6.40 | 15.76 | 4.27 | 10.69 | 5.22 | 7.29 | 2.54 | 13.93 | 3.87 |
| 6 | 11.90 | 3.63 | 4.69 | 2.90 | 46.66 | 8.88 | 18.26 | 5.92 | 12.98 | 5.79 | 9.49 | 3.10 | 16.83 | 5.67 |
| 7 | - | - | 5.28 | 3.22 | 54.84 | 11.79 | 22.95 | 7.86 | - | - | 12.04 | 3.65 | 18.05 | 6.68 |

Table 6: Formulation of 50 g gel containing 0.1% adapalene and 2.5% benzoyl peroxide

| Ingredients | Content (% w/w) | Calculated amount for 50 g (g) |
|---|---|---|
| Adapalene | 0.10 | 0.05 |
| Benzoyl peroxide | 2.50 | 1.25 |
| Propylen glycol | 4.00 | 2.00 |
| Glycerin | 4.00 | 2.00 |
| Sodium docusate | 0.05 | 0.025 |
| Poloxamer 188 | 0.20 | 0.10 |
| Simulgel SMS 88 | 6.00 | 3.00 |
| Purified water | 83.15 | 41.58 |

Sensory evaluation of selected gelling agents: Simulgel SMS 88, white gel, soft and smooth, non-greasy or sticky, easily spreadable, rapidly forms gel in water. Sepineon, similar characteristics to Simulgel SMS 88. NaCMC, transparent, thick gel with a soft and smooth texture, easily spreadable, produces foam during dispersion. Carbomer 940, transparent gel, soft texture, easily spreadable, non-greasy, requires neutralization with triethanolamine (TEA), pH difficult to precisely adjust. Xanthan gum, sticky on the skin, uncomfortable, forms clumps during dispersion in water.

Based on these evaluations, Simulgel SMS 88, Sepineon, NaCMC, and Carbomer 940 were selected for further testing and comparison with Product X. The results of the formulation screening are shown in Table 2.

According to Table 2, formulations F6, F8, F9, and F14 had a suitable skin-feel and pleasant application. These formulations were selected for drug release testing. The drug release results of formulations F6, F8, F9, and F14 are shown in Table 3:

According to Tables 2 and 3, the drug release rates of formulation F6 (containing Simulgel SMS 88) and F8 (containing Sepineon) both exceeded 95%, and their pH values ranged between 4.5 and 7, meeting the evaluation criteria. Formulations F6 and F8 were selected for further investigation of auxiliary excipients aimed at enhancing in vitro permeation and improving product characteristics. The excipient groups evaluated included penetration enhancers, humectants, surfactants, and pH stabilizers. The concentration of the penetration enhancer propylene glycol (PG) was studied at 2%, 4%, and 8%, in combination with gelling agents Simulgel SMS 88 (6%) and Sepineon (4%) at respective concentrations of 4% and 8%. The surfactant poloxamer 188 was investigated at concentrations ranging from 0.1% to 0.4%, with the optimal concentration selected based on visual assessment of active ingredient dispersion under fixed stirring time, temperature, and speed. The poloxamer 188 concentration was increased until the drug was homogeneously dispersed in the aqueous phase under identical mixing conditions.

Based on the preliminary in vitro permeation results, formulation F8 did not meet the performance criteria compared to product X and was therefore excluded from further testing. The formulations incorporating auxiliary excipients based on F6 and the corresponding quantification results are presented in Table 4.

According to Table 4, all F6-based formulations containing auxiliary excipients met the content requirements for both active ingredients. *In vitro* permeation studies were subsequently conducted for both drugs. The evaluation results are presented in Table 5.

According to Table 5, there were observable differences in the in vitro permeation profiles among the tested formulations. Specifically, formulation F6.3 exhibited the highest permeation for both active ingredients, with 52.84% of adapalene (AD) and 11.79% of benzoyl peroxide (BO) released after 7 hours. Among the formulations containing 4% glycerin (F6.1, F6.3, and F6.5), in vitro permeation varied depending on the concentration of propylene glycol. F6.3, which contained 4% propylene glycol, showed higher permeation compared to F6.1 (2% PG) and F6.5 (8% PG). Similarly, for the formulations with 8% glycerin (F6.2, F6.4, and F6.6), F6.4, containing 4% PG, demonstrated higher in vitro permeation of both active ingredients than the other two. An increase in glycerin concentration from 4% to 8% resulted in a decrease in in vitro permeation of both AD and BO. Among all tested formulations, F6.3 showed the highest permeation performance.

When comparing the in vitro permeation of F6.3 to reference product X, the results showed that after 7 hours, F6.3 provided superior permeation of both active ingredients. These findings indicate that F6.3 meets the initial formulation criteria and is comparable to product X in terms of drug release and in vitro permeation.

Therefore, formulation F6.3 satisfies the established requirements and demonstrates equivalence to product X regarding drug release and in vitro permeation. The complete formulation for a 50 g batch of gel is presented in Table 6.

The finished gel product met the quality requirements, as shown in Table 7.

*Preliminary Stability Results*

The gel formulation contains Adapalene 0.1% and Benzoyl Peroxide 2.5%, packaged in 10 g brown glass jars. The product is stored under ambient conditions at a temperature not exceeding 30 °C, in a cool place, protected from light. The primary packaging consists of neutral brown glass jars with a thickness of 1 mm, a diameter of 35 mm, and a height of 33 mm, sterilized by moist heat at 121 °C for 30 minutes

Table 7: Quality evaluation of the final product

| No. | Specification | Acceptance Criteria | Results |
|---|---|---|---|
| 1 | Appearance | Smooth, soft, pleasant, easy to rinse | Pass |
| 2 | pH | 4.5 - 7 | 6,24 ± 0,1 (pass) |
| 3 | Homogeneity | No particles in ¾ samples | Pass |
| 4 | Viscosity (cps) | 388000-429000 | 411542 ± 15 (pass) |
| 5 | Spreadability (cm) | 4.3-4.8 cm | 4,60 ± 0,7 (pass) |
| 6 | Drug Release | > 95% for both active ingredients after 2 hours | AD (96,85%) BO (96,68%) Pass |
| 7 | *In Vitro* Permeability | Equivalent to or higher than product X | 52.84% AD and 11.79% BO vs. 18.05% AD and 6.68% BO from product X after 7 h – Pass |
| 8 | Assay (%) | 90-110% (AD); 90-125% (BO) | AD (99.67%); BO (103.91%) - Pass |

Table 8: Quality Control Results for Sample 01 (Accelerated Conditions for 6 Months)

| Storage | | Appearance | pH | Homogeneity | Spreadability | Viscosity (cps) | Assay (%) | |
|---|---|---|---|---|---|---|---|---|
| Time (months) | Condition | | | | | | | |
| | Accelerated Conditions for 6 Months | Smooth, soft, pleasant on the skin, and easy to rinse off | 4.5-7 | No particles were observed in 3 out of 4 microscopic preparations | 4.3-4.8 cm | 388000-429000 cps | 90-110% (AD); 90-125% (BO | |
| | | | | | | | AD | BO |
| Initial | 40°C ± 2°C, 75% ± 5% RH | Pass | 6.76 ± 0.05 | Pass | 4.6 ± 0.1 | Pass | 98.59 | 105.21 |
| 3 | | Pass | 6.88 ± 0.05 | Pass | 4.7 ± 0.1 | Pass | 97.26 | 104.67 |
| 6 | | Pass | 6.67 ± 0.05 | Pass | 4.6 ± 0.1 | Pass | 99.76 | 106.22 |

and subsequently dried. Each jar is sealed with a black PVC plastic cap and a self-adhesive membrane to prevent air penetration, then placed in a cardboard carton box. One batch was subjected to accelerated stability testing for 6 months at 40 °C and 75% relative humidity, with sampling at 0, 3, and 6 months. Testing and acceptance criteria followed validated storage conditions and analytical methods. Samples were withdrawn from the storage chamber prior to each testing point and stored at 5 °C until analysis, which was conducted within four weeks of removal. The finished product testing results are presented in Table 8.

Based on the test results, it can be concluded that the gel formulation containing Adapalene 0.1% and Benzoyl Peroxide 2.5% remained physically and chemically stable after 6 months under accelerated storage conditions (40 °C / 75% RH). The physical characteristics, including appearance and texture, showed no noticeable changes, and the chemical stability was confirmed by consistent active ingredient content over time. These findings indicate that the product maintains its quality under stress conditions, supporting the recommendation for labeling the storage condition as “store below 30 °C.”

## CONCLUSION

This study successfully developed the formulation and manufacturing process for a gel containing Adapalene 0.1% and Benzoyl Peroxide 2.5%. The product was found to be comparable to Product X in several parameters, notably in vitro skin permeation and drug release—both of which are important indicators for assessing bioequivalence in future studies.

Regarding the formulation, the gel employed Simulgel SMS 88 as the hydrophilic gel base—a multifunctional excipient composed of sodium acrylate/acryloyldimethyltaurate/dimethyl acrylamide crosspolymer, isohexadecane, and polysorbate 60. Simulgel SMS 88 is a novel liquid emulsifying polymer widely used for its thickening, stabilizing, and structuring properties, producing soft gels with a non-greasy feel. It also helps maintain viscosity over time and functions effectively across a broad pH range, making it a promising excipient for topical preparations.

Additionally, the roles of propylene glycol and glycerin in enhancing drug release and in vitro permeation were evaluated through various formulations. The results suggest that the inclusion of these ingredients in topical gel formulations can improve therapeutic performance. The developed formulation shows potential for scale-up and application in future commercial manufacturing.

***Acknowledgments***

This research was funded by the Vietnam National University – Ho Chi Minh City (VNU-HCM) under project code C2020-44-04.

## REFERENCES

1. Decker A, Graber EM. Over-the-counter acne treatments: a review. The Journal of clinical and aesthetic dermatology. 2012;5(5):32.
2. Sagransky M, Yentzer BA, Feldman SR. A review of its current use in the treatment of acne vulgaris. Expert opinion on pharmacotherapy. 2009;10(15):2555-62. DOI: 10.1517/14656560903277228

3. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. The lancet. 2012;379(9813):361-72. DOI: 10.1016/S0140-6736(11)60321-8.
4. Chandira R, Pradeep PA, Bhowmik D, Chiranjib JB, Tripathi K, Sampath Kumar K. Design, development and formulation of antiacne dermatological gel. Journal of Chemical and Pharmaceutical Research. 2010;2(1):401-14.
5. Lei L, Bai Y, Qin X, Liu J, Huang W, Lv Q. Current Understanding of Hydrogel for Drug Release and Tissue Engineering. Gels. 2022;8(5). DOI: 10.3390/gels8050301
6. Berson DS, Shalita AR. The treatment of acne: the role of combination therapies. Journal of the American Academy of Dermatology. 1995;32(5):S31-S41. DOI: 10.1016/0190-9622(95)90418-2
7. Capizzi R, Landi F, Milani M, Amerio P. Skin tolerability and efficacy of combination therapy with hydrogen peroxide stabilized cream and adapalene gel in comparison with benzoyl peroxide cream and adapalene gel in common acne. A randomized, investigator-masked, controlled trial. British Journal of Dermatology. 2004;151(2):481-4. DOI: 10.1111/j.1365-2133.2004.06067.x.
8. Keating GM. Adapalene 0.1%/benzoyl peroxide 2.5% gel: a review of its use in the treatment of acne vulgaris in patients aged ≥ 12 years. American journal of clinical dermatology. 2011;12:407-20. DOI: 10.2165/11208170-000000000-00000
9. Nguyen V-H, Pham T-Q, Bui T-P, Thai T-T, Pham N-Q, Ly L-D, et al. Development and validation of a HPLC method for simultaneous quantitative determination of adapalene and benzoyl peroxide in gel products. Science and Technology Development Journal: Health Sciences. 2020;1(2):64-74.
10. Shrivastava B. Topical combination delivery of benzoyl peroxide and adapalene niosomal gel for acne treatment. Asian Journal of Pharmaceutics (AJP). 2019;13(04). DOI: 10.22377/ajp.v13i04.3409
11. Jain S, Kale DP, Swami R, Katiyar SS. Codelivery of benzoyl peroxide & adapalene using modified liposomal gel for improved acne therapy. Nanomedicine. 2018;13(12):1481-93. DOI: 10.2217/nnm-2018-0002
12. Ministry of Health. Vietnamese Pharmacopoeia V - Appendix 1.12 – Topical and Mucosal Preparations. The Medical Publisher; 2017. p. 18.
13. USP C. Adapalene Gel Monographs-United States Pharmacopeoa and National Formulary (USP 40 - NF 35). 2017.
14. USP C. Benzoyl Peroxide Gel Monographs-United States Pharmacopeoa and National Formulary (USP 40 - NF 35). 2017. p. 2988.