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Development of Anti-Acne Nanogel and Gel Formulations from Microwave-Assisted Extract of *Phyllanthus emblica*: Antioxidant–Antibacterial Potency, and Stability Evaluation

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Abstract: *Phyllanthus emblica* L. is known for its high phenolic and flavonoid content, which provides potent antioxidant and antibacterial effects. Acne vulgaris, caused by pathogenic bacteria, is a common dermatological condition. Natural treatments using bioactive compounds present a more desirable alternative. This study aimed to determine the total phenolic and flavonoid contents of P. emblica extract obtained by Microwave-Assisted Extraction, assess its antioxidant capacity and antibacterial activity, and formulate the extract into anti-acne nanogel and gel formulations. The nanogel and gel physical characteristics, stability, and antioxidant and antibacterial activities were studied in vitro. P. emblica fruit was extracted using microwave-assisted extraction with ethanol. Total phenolic and flavonoid contents were measured using the Folin-Ciocalteu and AlCl3 methods, antioxidant activity by DPPH assay, and antibacterial activity against P. acnes and S. epidermidis by agar diffusion. Nanogel (3, 5, 7%) and 7% gel formulations were tested for stability and bioactivity. The extract yielded 63.23 mg GAE/g of phenolic content and 6.20 mg QE/g of flavonoid content, with strong antioxidant (IC50 = 4.16 µg/mL) and antibacterial activity (inhibition zones: 12.73 mm for P. acnes and 15.54 mm for S. epidermidis). The 7% nanogel had a pH of 5.35, viscosity of 3738.63 cP, spreadability of 5.38-6.88 cm, and IC50 of 71.20 µg/mL, with inhibition zones of 15.33 mm and 18.51 mm for P. acnes and S. epidermidis, respectively. The 7% gel had a pH of 5.39, viscosity of 3991.13 cP, spreadability of 5.28-6.75 cm, IC50 of 93.50 µg/mL, and inhibition zones of 12.73 mm and 15.54 mm. P. emblica extract showed strong antioxidant and antibacterial effects, with nanogel and gel formulations displaying effective characteristics for natural acne treatment, supported by stability over 12 weeks.

Keywords: Antibacterial; Antioxidant, Microwave-Assisted Extraction, *Phyllanthus emblica*, Nanogel Formulation.

Introduction

The extraction methods can be classified into two primary categories: conventional and non-conventional. Variations in extraction techniques can affect the quantities and concentrations of substances obtained. Microwave-assisted extraction (MAE) is a commonly employed non-conventional extraction method. This extraction technique utilises microwave radiation to heat the solvent quickly and efficiently, enabling the extraction of compounds from plant materials, including phenolics, flavonoids, pectin, and oils. Compared to conventional extraction methods, MAE can increase the extract yield using less solvent and shorter extraction time. This method is a more modern, efficient, low-energy, and environmentally friendly alternative. Microwave radiation in MAE can penetrate the cell walls of herbal medicine and evenly excite fat and water molecules, thereby increasing the yield of crude extract and attracting more metabolite compounds, such as phenolics [1,2].

Phenolic and flavonoid compounds are plants' largest compounds that act as natural antioxidants. Phenolics have a phenol ring with an easily oxidised hydroxyl group, so they can donate hydrogen atoms to free radicals and form stable phenoxy radicals, making them potential antioxidants. Many medicinal plants contain high levels of antioxidants, especially phenolic compounds such as flavonoids and phenolic acids, which play important roles in biological and pharmacological activities, making them relevant for treating and preventing diseases [3]. The close relationship between the antioxidant and antibacterial activities of phenolic and flavonoid compounds makes them a focus of research as natural solutions for treating diseases caused by free radicals and bacterial infections, including acne caused by *Propionibacterium acnes* and *Staphylococcus epidermidis*. Acne is a common skin problem, affecting 85% of the world's population aged 11-30 years, with a prevalence in Indonesia reaching 80-85% in adolescents and 12-3% in adult women [4–6].

Anti-acne treatments are effective because they can correct abnormalities in hair follicles, reduce the number of bacterial colonies that cause acne, reduce skin irritation, control excessive sebum production, and help remove dead skin cells to prevent bacteria from building up. Acne treatment usually involves antibiotics, but long-term use can cause side effects such as skin irritation and antibiotic resistance. Therefore, using natural ingredients as an alternative acne treatment is a safer choice

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with lower side effects. Compounds with antioxidant and antibacterial activities, such as phenolics and flavonoids, can be important in acne treatment. Antioxidant activity can neutralise free radicals that can trigger skin inflammation, while antibacterial activity can effectively inhibit the growth of *Propionibacterium acnes* and *Staphylococcus epidermidis*, two main bacteria that cause acne [7–9]. One of the plants rich in polyphenols, with antioxidant and antibacterial properties, and widely distributed in Asia, is *Phyllanthus emblica*.

Phyllanthus emblica is widely distributed across Southeast Asia, including Indonesia, and is found in natural habitats in Java, Sumatra, Kalimantan, Maluku, and Nusa Tenggara. This fruit is traditionally consumed for its sweet and slightly astringent taste and is well recognised for a broad range of pharmacological properties, including antioxidant, antimicrobial, antidiabetic, cardioprotective, anticancer, and anti-inflammatory activities. Previous studies have identified several key bioactive constituents in *P. emblica*, such as ellagitannins, gallotannins, anthocyanins, vitamin C, mucic acid, and various phenolic acids.

The selection of *Phyllanthus emblica* in this study is scientifically justified by its rich profile of polyphenolic and flavonoid compounds, which are strongly associated with antioxidant mechanisms and antibacterial activity, two fundamental aspects of acne management. Acne vulgaris involves oxidative stress, inflammation, and colonisation by *Propionibacterium acnes* and *Staphylococcus epidermidis*. The phytochemical composition of *P. emblica* directly targets these pathways through free radical scavenging, inhibition of microbial growth, and modulation of inflammatory responses. Furthermore, its wide availability in Indonesia supports its potential development into affordable, natural anti-acne formulations. Therefore, *Phyllanthus emblica* offers a rational, evidence-based foundation for the development of antioxidant and antibacterial gel and nanogel preparations for acne treatment [10–12].

Nanogels represent an advanced topical delivery system compared with conventional gels. While traditional gels offer good stability, ease of application, and high-water content, their ability to enhance dermal penetration of active compounds is often limited. Nanogels are polymeric hydrogel systems with particle sizes in the nanometer range, which have been reported to improve skin permeation and dermal deposition of active substances compared with conventional gel formulations. This enhancement is mainly attributed to their small size, high surface area, and deformable polymeric network, which facilitates closer contact with the stratum corneum and promotes more efficient diffusion of active compounds into the skin layers. These characteristics make nanogels promising carriers for topical delivery of antioxidant and anti-acne agents [13,14].

Growing evidence indicates that oxidative stress and bacterial dysbiosis are central mechanisms in acne pathogenesis. Excessive free radicals enhance inflammatory cascades in pilosebaceous units, while Cutibacterium *acnes* and *Staphylococcus epidermidis* proliferation aggravates follicular obstruction and inflammation. The World Health Organization (WHO) identifies common skin diseases, including acne, as among the most prevalent non-communicable dermatological conditions globally, contributing substantially to morbidity and impairment of quality of life. Because oxidative stress and bacterial colonisation are two of the most critical and well-defined therapeutic targets in acne, this study focused specifically on evaluating antioxidant and antibacterial activities as primary indicators of anti-acne potential. These assays are mechanistically relevant, widely validated in dermatological research, and directly reflect the core pathophysiological processes underlying CNE development [15].

This study aimed to perform phytochemical screening and characterisation of simplicia and ethanol extracts of *Phyllanthus emblica* fruit, including identification of functional groups using Fourier Transform Infrared Spectroscopy (FTIR). Extraction was conducted using the Microwave-Assisted Extraction (MAE) technique, and the resulting extract was evaluated for total phenolic content (Folin–Ciocalteu method), total flavonoid content ($AlCl_3$ method), and antioxidant activity (DPPH). Antibacterial activity was examined using the agar well diffusion method against *Propionibacterium acnes* and *Staphylococcus epidermidis*. The ethanol extract was subsequently formulated into topical anti-acne gel and nanogel preparations to compare their performance. Each formulation was evaluated for organoleptic properties, homogeneity, pH, viscosity, and spreadability, followed by stability assessment through room-temperature storage and cycling tests. Post-stability analyses included re-evaluation of pH, viscosity, and organoleptic characteristics. Both formulations were further tested for antioxidant and antibacterial activities to assess their therapeutic potential and to compare the overall effectiveness of the gel and nanogel systems.

Materials and Methods

Plant Material Collection and Sample Preparation

Fresh fruits of *Phyllanthus emblica* L. were collected from Padang Lawas Regency, North Sumatra, in August 2023. Etti Sartina Siregar carried out species authentication at the Plant Systematics Laboratory, Herbarium Medanense (MEDA), Faculty of Mathematics and Natural Sciences, Universitas Sumatera Utara. The plant was confirmed morphologically as *Phyllanthus emblica* L., and a voucher specimen was deposited under the reference number 1360/MEDA/2023, where it is permanently stored for future verification. After authentication, the fruits were washed, cut, weighed, and dried until brittle, then ground into a fine powder and stored. Extraction was performed by mixing the dried powder with ethanol at a 1:20 ratio, then microwave-assisted extraction (450 W, 14 minutes). The filtrate was concentrated using a rotary evaporator at 50–55°C and further dried in an oven at 40°C to obtain a thick ethanolic extract [16].

Phytochemical Screening and Characterisation

Characterisation of Simplicia and *Phyllanthus emblica* fruit extracts includes determining water content, water-soluble and ethanol-soluble extract content, and total ash and acid-insoluble ash content. Phytochemical screening was also carried out to identify the content of alkaloids, flavonoids, tannins, saponins, steroids/triterpenoids, and glycosides in Simplicia powder. In addition, simplicia and extracts were characterised by Fourier Transform Infrared Spectroscopy (FTIR) to identify the functional groups of bioactive compounds present in the extracts[12,17].

Determination of Total Phenol and Total Flavonoid Content

The total phenolic content was determined using the Folin–Ciocalteu method by reacting 0.3 mL of sample with distilled water, 10% Folin–Ciocalteu reagent, and 20% Na_2CO_3, followed by 30 minutes of incubation at room temperature. Absorbance was measured at 400–800 nm and expressed as mg gallic acid equivalents per gram of sample. Total flavonoid content was assessed by mixing 0.5 mL of the sample with methanol, 10% $AlCl_3$, 1 M sodium acetate, and distilled water, then incubating for 47 minutes at room temperature. The absorbance was recorded at 437 nm [18].

Antioxidant Testing of Extracts

A 10 mg portion of the extract was dissolved in methanol to prepare a 1000 µg/mL stock solution, which was subsequently diluted to 10 µg/mL. Aliquots of 0.5–2.0 mL were transferred into 5 mL volumetric flasks to obtain working concentrations of 1–4 µg/mL. Each solution was mixed with 1 mL of 200 µg/mL DPPH and brought to volume with methanol. After homogenisation, the mixtures were incubated for 26 minutes at room temperature, and absorbance was measured at 516 nm. Antioxidant activity was expressed as percent inhibition, and the IC_{50} value was determined by linear regression [18].

Antibacterial testing of extracts

Colonies of *Propionibacterium acnes* and *Staphylococcus epidermidis* were cultured in Nutrient Broth and incubated at 37 °C until the turbidity reached <25% transmittance at 580 nm. The *Phyllanthus emblica* extract was prepared by dissolving 5 g of extract in DMSO to obtain a 500 mg/mL stock, which was then diluted stepwise to 0.5 mg/mL. Antibacterial activity was evaluated using the agar well diffusion method. A 0.1 mL bacterial inoculum was mixed with 15 mL of molten MHA, solidified, and perforated with 6 mm wells. Each well received 25 µL of test solutions at various concentrations, using DMSO as a negative control and Clidacor® as a positive control. Plates were incubated at 37 °C for 24 hours, and inhibition zone diameters were measured to assess antibacterial activity [5].

Formulation of Extract Nanogel and Gel Preparation

Five formulations were prepared to evaluate the anti-acne activity of *Phyllanthus emblica* fruit ethanol extract in both nanogel and gel forms. The formulations included a blank nanogel without extract (F0), nanogels containing 3% (F1), 5% (F2), and 7% (F3) concentrations of *Phyllanthus emblica* ethanol extract, and a gel with 7% extract (F4). These formulations were developed to assess the effect of extract concentration and particle size on the anti-acne activity. The composition of each formulation was based on a consistent base, comprising Carbopol 940, hydroxypropyl methylcellulose (HPMC), triethanolamine (TEA), glycerin, propylene glycol, methyl paraben, propyl paraben, and distilled water, with specific adjustments for extract concentration and gelling agents.

The 7% concentration was selected as optimal based on preliminary antibacterial testing, where it demonstrated strong inhibition zones, indicating significant anti-acne potential. In addition, a preliminary formulation orientation study was conducted, which showed that extract concentrations above 7% resulted in formulations that did not meet physical evaluation criteria, particularly in terms of homogeneity and viscosity. Therefore, extract concentrations of 3%, 5%, and 7% were selected to ensure effective antibacterial activity while maintaining acceptable physical characteristics of the nanogel and gel formulations. The detailed formula compositions for each formulation are presented in Table 1.

Table (1): Nanogel and Gel formula composition.

Ingredients	F0	F1	F2	F3	F4
Phyllanthus emblica fruit extract	0	3	5	7	7
Carbopol 940	1	1	1	1	1,25
HPMC	0,25	0,25	0,25	0,25	-
TEA	1	1	1	1	1
Glycerin	10	10	10	10	5
Propylene glycol	3	3	3	3	10
Methylparaben	0,2	0,2	0,2	0,2	0,2
Propylparaben	0,02	0,02	0,02	0,02	0,02
Aquades	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100

The nanogel formulation of *Phyllanthus emblica* fruit extract began by heating a mortar and pestle in hot water for 10 minutes, followed by drying. Hot distilled water was added to the first mortar, and Carbopol 940 was gradually mixed in, allowing it to hydrate for 24 hours. In a separate mortar, HPMC was similarly hydrated. After 24 hours, both Carbopol 940 and HPMC were blended until homogeneous. TEA and glycerin were added to the first mortar, then triturated to achieve a uniform mixture. Methyl paraben and propyl paraben, dissolved in propylene glycol, were added to the second mortar and mixed thoroughly before being incorporated into the first mortar with continuous mixing. The extract was then added, followed by distilled water to reach a final weight of 100 g, and the mixture was homogenized at 2000 rpm for 2 hours, then stirred for another 2 hours. For the gel formulation, ingredients were weighed using a digital scale. Carbopol was hydrated in hot distilled water for 24 hours, and methyl paraben was dissolved in propylene glycol (Mixture 1). In a separate mortar, the extract was triturated until smooth. After Carbopol hydration, TEA was added gradually to form the gel base, followed by glycerin and Mixture 1, all combined to achieve homogeneity. Finally, 7% extract was added, followed by the gradual addition of distilled water to ensure uniform texture [19,20].

Evaluation of Extract Nanogel and Gel Preparation

The quality evaluation of the *Phyllanthus emblica* extract nanogel and gel formulations included assessments of organoleptic properties, homogeneity, pH, viscosity, spreadability, and particle size. Organoleptic characteristics, appearance, color, and odor were examined visually to ensure acceptable aesthetic and sensory attributes. Homogeneity was assessed by spreading a small amount of the formulation onto a glass slide to confirm uniformity, with no visible granules or phase separation [21–23].

The pH of each preparation was measured using a calibrated pH meter, previously adjusted with buffer solutions at pH 7.01 and pH 4.01. The electrode was rinsed, dried, and immersed in the sample until a stable Reading was obtained. Viscosity was determined using a Brookfield viscometer (NDJ-8S), where 100 g of the formulation was placed in a cylindrical container, spindle number 4 was immersed, and readings were recorded upon reaching stability [21–23].

Spreadability was evaluated by placing 0.5 g of the formulation between two glass plates, allowing it to rest for 1 minute, and subsequently applying incremental weights (25–125 g). The resulting spread diameter was measured to assess ease of topical application. Particle size analysis of the nanogel formulation was performed using a particle size analyzer (Fritsch Analysette 22 NanoTec) to determine the particle size distribution and confirm suitability for dermal penetration and product stability [21–23].

Evaluation of Nanogel and Gel Preparation Stability

The stability of both *Phyllanthus emblica* nanogel and gel preparations was evaluated through storage at room temperature and cycling tests, with assessments of organoleptic properties, pH, and viscosity. Each formulation's stability was observed over 12 weeks at room temperature, with measurements taken at weeks 0, 2, 4, 6, 8, 10, and 12. Organoleptic evaluations involved assessing each preparation's appearance, color, and odor. pH measurements were performed using a calibrated pH meter (AZ Instrument 86502) with neutral (pH 7.01) and acidic (pH 4.01) buffer solutions. After cleaning and drying the electrode with distilled water, it was immersed in each sample until a stable Reading was obtained. Viscosity was measured using an NDJ-8S viscometer; 100 g of each sample was placed in the container with spindle 4, and measurements were recorded. Viscosity readings were taken at the same intervals as the pH measurements. The cycling stability test was performed by alternating between 4±2°C for 24 hours and

40±2°C for 24 hours. Each cycle included both temperature conditions, repeated 6 times. Stability assessments for each cycle included organoleptic observations, pH measurements, and viscosity tests, conducted both before and after cycling to detect changes due to temperature variations [21–23].

Antioxidant Activity Testing of Extract Nanogel and Gel Preparations

The antioxidant activity of the extract-loaded nanogel and gel preparations was evaluated using the DPPH method. Each formulation (10 mg) was dissolved in methanol to obtain a 1000 µg/mL stock solution, which was subsequently diluted to 10 µg/mL. Aliquots of 0.5, 1.0, 1.5, and 2.0 mL of this solution were transferred into 5 mL volumetric flasks to obtain working concentrations of 1–4 µg/mL. Each sample was then mixed with 1 mL of 200 µg/mL DPPH solution and adjusted to volume with methanol, followed by incubation for 26 minutes at room temperature. Absorbance was recorded at 516 nm, and antioxidant activity was expressed as the percentage of DPPH radical inhibition. The IC_{50} value was calculated using linear regression. Quercetin served as the positive control, while methanol (the solvent used for sample preparation) served as the negative control; both were tested in parallel with all samples to ensure method validation [18].

Antibacterial Activity Testing of Extract Nanogel and Gel Preparations

The antibacterial activity of the nanogel and gel preparations was determined using the agar well diffusion method. Bacterial inocula of *Staphylococcus epidermidis* and *Propionibacterium acnes* (0.1 mL each) were introduced into separate sterile petri dishes, followed by the addition of 15 mL of molten Mueller-Hinton Agar (MHA), which was then allowed to solidify. Wells of 6 mm diameter were created using a sterile cork borer, and each well was filled with 25 µL of the *Phyllanthus emblica* extract-containing nanogel or gel preparation. Clidacor® (clindamycin phosphate 1% gel) was used as the positive control, while DMSO (the solvent used for extract dissolution) served as the negative control. All plates were incubated at 37 °C for 24 hours. After incubation, the diameter of the inhibition zone surrounding each well was measured using a vernier caliper to determine antibacterial activity [5].

Skin Irritation Test on Human Volunteers

A skin irritation test was conducted on human volunteers to evaluate the safety of the nanogel formulation for topical application. The study protocol was approved by the Health Research Ethics Committee of Universitas Sumatera Utara (Ethical Clearance No. 256/KEPK/USU/2024), and all participants provided written informed consent prior to enrolment.

The irritation assessment was performed using an open patch test method. A defined area (2.5 × 2.5 cm) on the inner forearm of each volunteer was selected as the application site. The nanogel formulation containing *Phyllanthus emblica* fruit extract at the highest tested concentration (7%) was applied evenly to the designated area and left uncovered. The application was performed twice daily for three consecutive days. The treated skin area was observed for any signs of irritation, including erythema, itching, or swelling. Skin reactions were recorded qualitatively, where the presence of any irritation response was marked as positive (+), and the absence of reactions was marked as negative (–), following established cosmetic safety evaluation guidelines.

The inclusion criteria comprised healthy female volunteers aged 20–35 years, with no history of allergic skin conditions, and who were willing to participate in the study. Exclusion criteria included pregnancy or lactation, dermatological disorders, current illness, use of oral or topical medications that could affect skin condition, or refusal to participate in the irritation test.

Data Analysis

Statistical analysis was performed using IBM SPSS. All data are expressed as mean ± standard deviation. Normality was evaluated using an appropriate normality test. For datasets that met the assumption of normality, one-way ANOVA was applied; non-normally distributed data were analysed using the Kruskal–Wallis test.

Results and Discussion

Sample preparation

The identification results at the Medanese Herbarium, FMIPA, University of North Sumatra, showed that the plant used was *Phyllanthus emblica* L., a member of the Phyllanthaceae family. The preparation of the simplicia started with 15 kg of fresh fruit, and 1.5 kg of simplicia powder was obtained. Extraction used microwave-assisted extraction (MAE) with 96% ethanol solvent, followed by rotary evaporation at 50°C, yielding 252.43 g of extract from 491.81 g of powder, corresponding to 51.32%.

Phytochemical Screening and Characterisation

The characterisation process was carried out to determine the quality of the herbal medicine, as seen in Table 2.

Table (2): Characterisation Results of Simplicia and Extracts.

Parameter	Simplicia	Extract
Water content	6.67±1.15%	5.96 ± 0.02%
Water Soluble Essence Content	41.63±4.44%	-
Ethanol Soluble Essence Content	50.92 ± 2.70%	-
Total Ash Content	3.51 ± 0.07%	3.29 ± 0.48%
Acid Insoluble Ash Content	0.31±0.11%	0.24 ± 0.07%

The water content of *Phyllanthus emblica* fruit simplicia and extract was 6.67% and 5.96%, respectively, both meeting Herbal Pharmacopoeia standards (<10%). Low water content is crucial to minimize microbial contamination and physical degradation. Water-soluble and ethanol-soluble extract levels in simplicia were 41.63% and 50.92%, respectively, exceeding the Herbal Pharmacopoeia standards (≥16.2% for water, ≥10.6% for ethanol), indicating the presence of compounds like glycosides, sugars, proteins (water-soluble), flavonoids, saponins, and tannins (ethanol-soluble). Total ash content was 3.51% for simplicia and 3.29% for extract, while acid-insoluble ash was 0.31% and 0.24%, all within acceptable limits. Phytochemical screening identified flavonoids, glycosides, saponins, steroids/triterpenoids, and tannins in both the simplicia and extract, with no alkaloids detected. These secondary metabolites suggest antioxidant and antibacterial potential for both the herbal material and *Phyllanthus emblica* extract [12].

Table (3): Results of Phytochemical Screening of Simplicia and Extract.

Group.	Simplicia powder	Extract
Alkaloids	-	-
Flavonoids	+	+
Glycosides	+	+
Saponins	+	+
Steroids/Triterpenoids	+	+
Tannin	+	+

The FTIR spectra of *Phyllanthus emblica* samples, including the simplisia (crude drug), extract, and 7% nanogel formulations, reveal important insights into the functional groups present and changes in composition across these preparations. In the simplisia spectrum, a prominent broad absorption band at approximately 3352 cm^{-1} indicates the presence of hydroxyl (-OH) groups, which are commonly associated with phenolic compounds and carbohydrates. Additionally, an aliphatic C-H stretching band around 2927 cm^{-1} suggests the presence of lipids or other organic compounds with C-H bonds. A peak at

1639 cm⁻¹ corresponds to C=C or C=O stretching, typically found in aromatic or carbonyl compounds, indicating the presence of phenolic acids or other aromatic structures. Deformation vibrations in the 900-700 cm⁻¹ region further support the presence of aromatic compounds such as flavonoids, highlighting the bioactive potential of the simplisia [24].

The extract spectrum shows some modifications, particularly a reduction in the intensity of the hydroxyl band around 3456 cm⁻¹, suggesting the removal of water and certain hydroxyl compounds during extraction. However, the aliphatic C-H band at 2931 cm⁻¹ remains, indicating the persistence of aliphatic compounds. The consistent band at 1639 cm⁻¹ confirms the successful extraction and stability of key phenolic compounds, such as flavonoids. Additionally, a new band at 1255 cm⁻¹ in the extract spectrum may indicate the presence of esters or ethers, suggesting a shift or increase in specific compounds post-extraction. In the 7% nanogel spectrum, the essential functional groups from the extract, including hydroxyl, aliphatic, and aromatic groups, are retained, with similar peaks observed around 3367 cm⁻¹, 2935 cm⁻¹, 1618 cm⁻¹, and 1222 cm⁻¹. This similarity confirms the successful incorporation of bioactive compounds into the nanogel matrix, preserving the therapeutic properties of the *Phyllanthus emblica* extract. These findings indicate that the phenolic, flavonoid, and other functional components were effectively retained across the formulations, supporting the potential antioxidant and pharmacological efficacy of the nanogel preparation [24].

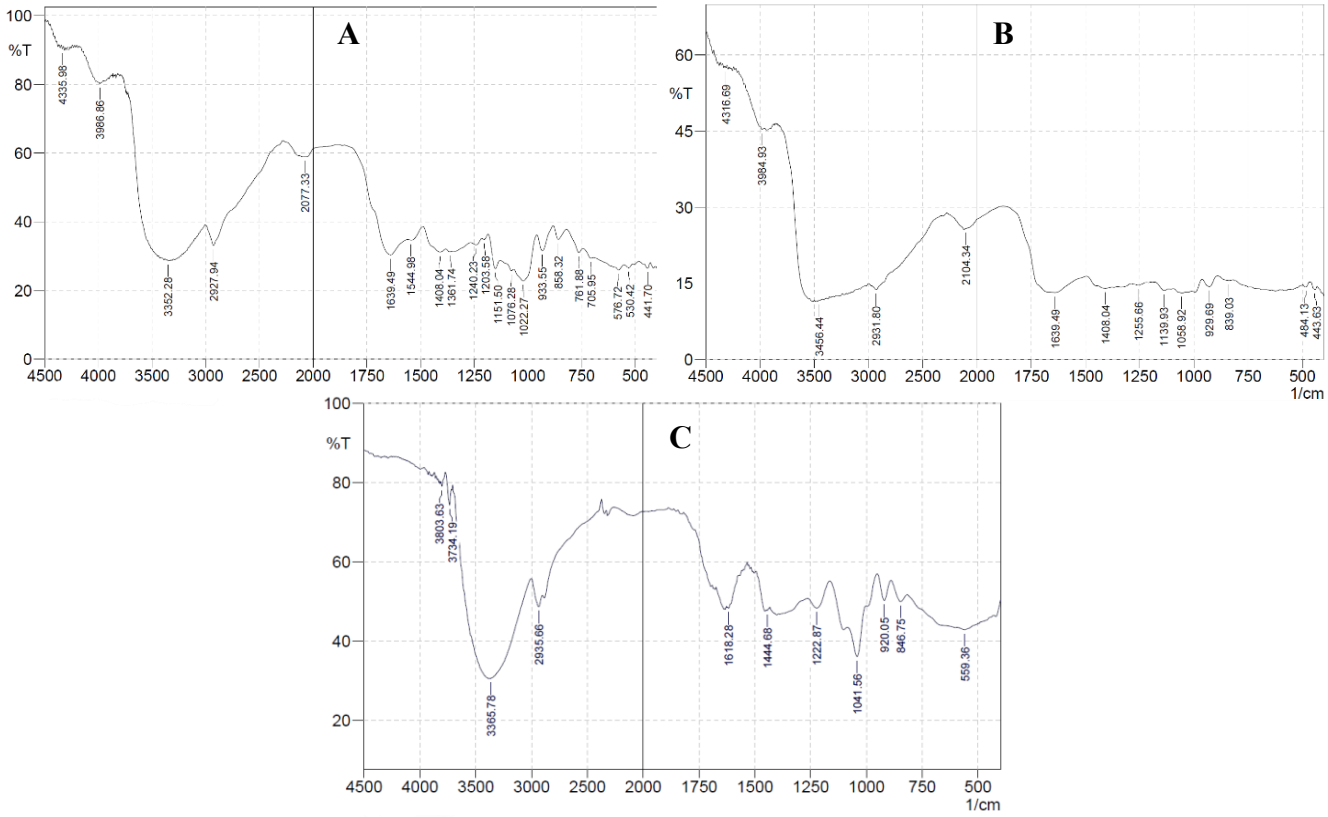

Figure (1): FTIR spectrum of A. Simplisia B. Extract C. Nanogel 7%

Results of Determination of Total Phenol, Flavonoid, and Antioxidant Activity

The total phenolic, flavonoid content, and antioxidant activity of the *Phyllanthus emblica* ethanol extract were quantified using UV–Vis spectrophotometry. The results are presented in Table 4.

Table (4): Results of Determination of Total Phenol and Flavonoid Content of Extract.

Parameter	Determination Results
Total phenol (mg GAE/g)	63.22±0.06%
Total Flavonoids (mg QE/g)	6.20±0.51%

The ethanol extract of *Phyllanthus emblica* exhibited a high total phenolic content of 63.22 ± 0.06 mg GAE/g, indicating that the fruit is a rich source of phenolic constituents. Phenolic compounds are well-recognized for their strong antioxidant capacity, primarily through hydrogen atom or electron donation to neutralize free radicals. Their ability to reduce oxidative stress suggests a potential role in preventing cellular damage associated with degenerative conditions, supporting the therapeutic value of *P. emblica* phenolics. The total flavonoid content measured 6.20 ± 0.51 mg QE/g, demonstrating the presence of substantial flavonoid levels. Flavonoids, as a significant subgroup of phenolics, contribute not only to antioxidant activity but also exhibit anti-inflammatory, antimicrobial, and cardioprotective effects. Their mechanisms, such as metal ion chelation, lipid oxidation inhibition, and modulation of pro-oxidant enzymes, further reinforce the biological relevance of *P. emblica* flavonoids in maintaining cellular integrity and enhancing overall skin health [25,26].

Table (5): Results of Antioxidant Activity.

Sample	IC_{50} (mean±SD)
Extract	4.16±0.44%
Quercetin (Positive Control)	8.58±2.93%

The antioxidant activity, assessed by the DPPH assay, yielded an IC_{50} value of 4.16 ± 0.44 µg/mL, demonstrating very strong free radical-scavenging activity. Notably, the extract showed stronger activity than quercetin, the positive control. This high antioxidant potency is consistent with the elevated phenolic and flavonoid concentrations quantified earlier. The strong scavenging activity indicates the extract's capability to mitigate oxidative stress effectively. From a dermatological perspective, this antioxidant strength is particularly relevant for anti-acne and anti-aging applications. Oxidative stress contributes to inflammation, sebum oxidation, and degradation of skin barrier

components. Thus, incorporating P. emblica extract into topical formulations may protect against UV-induced damage and environmental pollutants, making it a promising natural active ingredient for skincare products aimed at improving skin health and preventing premature aging [26,27].

Antibacterial Activity of Extract

The antibacterial assessment conducted using the agar well diffusion method demonstrated that the ethanol extract of *Phyllanthus emblica* fruit inhibited the growth of both *Propionibacterium acnes* and *Staphylococcus epidermidis*. The presence of clear inhibition zones surrounding the wells containing the extract confirmed its antibacterial activity. The detailed inhibition zone measurements are presented in Table 5.

Table (5): Results of Antibacterial Activity of Extracts.

Concentration of Extract (mg/ml)	Diameter of inhibition area (mm; n=3)	
	Propionibacterium acnes	***Staphylococcus epidermidis***
Clindamycin Phosphate 1%	23.68 ± 0.29	30.36 ± 0.35
500	21.11 ± 0.27	23.59 ± 0.21
100	14.83 ± 0.23	16.30 ± 0.26
90	14.16 ± 0.25	15.11 ± 0.35
80	12.93 ± 0.20	13.93 ± 0.32
70	12.26 ± 0.20	13.21 ± 0.29
50	11.37 ± 0.12	12.20 ± 0.36
30	10.71 ± 0.76	10.90 ± 0.36
15	9.98 ± 0.16	10.20 ± 0.36
5	8.92 ± 0.25	9.35 ± 0.47
2.5	8.20 ± 0.26	8.50 ± 0.40
1	-	-
0.5	-	-
Blank (DMSO)	-	-

The antibacterial activity of a substance is classified into four levels: weak (<5 mm), moderate (5-10 mm), strong (10-20 mm), and very strong (>20 mm). Based on the test results, *Phyllanthus emblica* extract inhibited the growth of *Propionibacterium acnes* and *Staphylococcus epidermidis*, with a strong effect at 30-100 mg/mL. The DMSO negative control did not show an inhibition zone, confirming that the antibacterial activity was due to the *Phyllanthus emblica* extract. The positive control using Clindamycin Phosphate 1% demonstrated significant antibacterial activity, confirming the validity of the test. The antibacterial activity of the extract increased with increasing concentration, with a larger inhibition zone diameter at higher concentrations [28,29].

The antibacterial activity of *the Phyllanthus emblica* ethanol extract increased with increasing concentration, as evidenced by a larger inhibition zone diameter. Conversely, lower concentrations produced smaller inhibition zones. The extract's antibacterial activity falls into the moderate category (inhibition zone diameter 5-10 mm) at concentrations of 2.5 -15 mg/mL. At higher concentrations, 15 - 500 mg/mL, the activity is classified as strong (inhibition zone diameter 10-20 mm). For the formulation of *Phyllanthus emblica* ethanol extract nanogel, three concentrations with strong antibacterial activity were selected: 30 mg/mL (FI), 50 mg/mL (FII), and 70 mg/mL (FIII). This selection aims to ensure that the nanogel formulation maintains high antibacterial efficacy, targeting *Propionibacterium acnes* and *Staphylococcus epidermidis*, common bacteria associated with acne. The inhibition zones observed for these bacteria, with *Staphylococcus epidermidis* generally showing larger zones than *Propionibacterium acnes*, suggest that the extract has a broad-spectrum antibacterial activity. The consistent increase in inhibition zone diameter with concentration further supports the extract's potential as an effective active ingredient in anti-acne treatments, particularly when formulated as a nanogel to enhance skin penetration and localized action [28,29].

Preparation and Evaluation of Extract Nanogel and Gel Preparations

The selection of *Phyllanthus emblica* extract concentrations for formulation (3%, 5%, and 7%) was based on the strong inhibition zones observed against *Propionibacterium acnes* and *Staphylococcus epidermidis*, as shown in Table 5. The highest concentration (7%) was chosen carefully, as higher extract levels tend to lower pH, potentially making the formulation more acidic. Maintaining the skin's pH within its tolerance range (4.5-6.5) is essential to prevent irritation. The 7% concentration was also used in the gel formulation to enable a direct comparison with the nanogel, as the nanogel is expected to provide superior antibacterial efficacy due to enhanced penetration and stability. The antibacterial performance of both nanogel and gel formulations is illustrated in Figure 2.

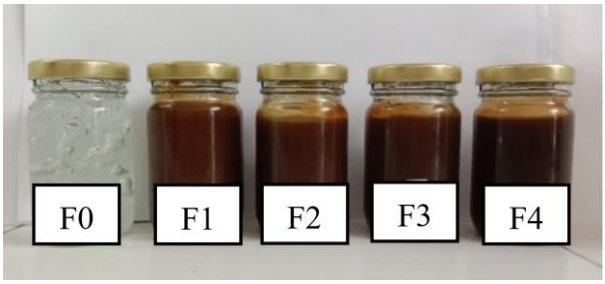

Figure (2): Nanogel and gel formulation.

The *Phyllanthus emblica* fruit extract nanogel and gel preparations were evaluated using several parameters, including organoleptic tests, homogeneity, pH, viscosity, spreadability, and particle Size. The results of this evaluation are shown in Table 6.

Table (6): Results of Nanogel and gel preparation evaluation tests.

Parameter	F0 (Nanogel Blank)	F1 (Nanogel 3%)	F2 (Nanogel 5%)	F3 (Nanogel 7%)	F4 (Gel 7%)
Color	Transparent	Blackish brown	Blackish brown	Blackish brown	Blackish brown
Odor	Distinctive odour	Distinctive odour	Distinctive odour	Distinctive odour	Distinctive odour
Consistency	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid
Homogeneity	Homogeneous 	Homogeneous 	Homogeneous 	Homogeneous 	Homogeneous 
pH Value	6.36 ± 0.01	5.91 ± 0.01	5.58 ± 0.01	5.35 ± 0.005	5.39 ± 0.005
Viscosity (cP)	9738.46 ± 4.56	6316.60 ± 10.09	4910.56 ± 1.97	3738.63 ± 0.40	3991.13 ± 0.64
Spreadability (cm) (0 g/125 g)	5.00 ± 0.05 / 6.01 ± 0.02	5.16 ± 0.02 / 6.26 ± 0.02	5.21 ± 0.02 / 6.48 ± 0.02	5.38 ± 0.07 / 6.88 ± 0.02	5.28 ± 0.02 / 6.75 ± 0.05
Particle Size (nm)	-	66	214	236	-

Mean ± SD: Values are presented as the mean with standard deviation (SD) from three replicates (n=3).

The organoleptic examination, which included assessments of color, odor, and consistency, revealed that F0 (blank nanogel) was transparent, while the nanogels with increasing concentrations of *Phyllanthus emblica* extract (F1, F2, F3) and the 7% gel (F4) exhibited a blackish-brown color, attributed to the extract. All formulations had a distinctive odor and a semisolid consistency, indicating that the extract primarily influenced color without altering texture. These results suggest that the formulations are aesthetically acceptable and likely to remain stable during storage, which is important for consumer acceptance. Homogeneity testing was conducted to ensure uniform distribution of ingredients in each formulation. All formulations (F0 to F4) demonstrated good homogeneity with no visible coarse particles, reducing the risk of skin irritation and ensuring consistent delivery of active ingredients. In topical applications, uniform formulations are essential for therapeutic efficacy, as inconsistencies could lead to variable effectiveness [21–23].

The pH values for the formulations ranged from 6.36 ± 0.01 (F0) to 5.35 ± 0.005 (F3), with F4 (7% gel) measuring 5.39 ± 0.005. The decline in pH with increasing extract concentrations aligns with the acidic nature of *Phyllanthus emblica* extract. All formulations fell within the skin's pH tolerance range of 4.5-6.5, indicating that they are unlikely to irritate. Maintaining a pH close to the skin's natural level is critical to ensure user comfort and prevent disruption of the skin barrier [21–23].

Viscosity measurements, which reflect the thickness of the formulations, showed that F0 (blank nanogel) had the highest viscosity (9738.46 ± 4.56 cP), which decreased as the extract concentration increased, with F3 (7% nanogel) at 3738.63 ± 0.40 cP and F4 (7% gel) at 3991.13 ± 0.64 cP. All values were within the ideal range for gel formulations (2000-50,000 cP), indicating that the formulations can be easily applied to the skin without being too runny or too thick. Appropriate viscosity is essential for ensuring a comfortable, spreadable consistency that maintains skin contact and enhances therapeutic efficacy [21–23].

The spreadability test, used to determine how well a formulation spreads across the skin, showed that spreadability ranged from 5.00 ± 0.05 cm (F0) to 6.88 ± 0.02 cm (F3) under a 125 g load. F4 (7% gel) demonstrated spreadability between 5.28 ± 0.02 cm and 6.75 ± 0.05 cm, which is within the ideal range. Good spreadability ensures that the formulation can be easily and evenly applied, maximizing skin contact and thereby enhancing its therapeutic potential [21–23].

Evaluation of Nanogel and Gel Preparation Stability

The stability of the *Phyllanthus emblica* fruit ethanol extract Nanogel and gel preparation was evaluated by observing several main parameters, namely organoleptic, pH, and viscosity, which were evaluated for 12 weeks of storage at room temperature and cycling tests at extreme temperatures. The results of this stability evaluation test are shown in Table 7, and those of this cycling test are shown in Table 8.

Table (7): Results of the Nanogel and Gel Preparation Stability Evaluation Test at Room Temperature.

Formula	Week	Colour	Odor	Consistency	pH (Mean ± SD)	Viscosity (cP) (Mean ± SD)
F0	0	Transparent	Distinctive odour	Semisolid	6.36 ± 0.01	9738.46 ± 4.56
	12	Transparent	Distinctive odour	Semisolid	6.18 ± 0.01	9572.16 ± 0.68
F1	0	Blackish brown	Distinctive odour	Semisolid	5.91 ± 0.01	6316.60 ± 10.09
	12	Blackish brown	Distinctive odour	Semisolid	5.71 ± 0.01	6016.10 ± 0.76
F2	0	Blackish brown	Distinctive odour	Semisolid	5.58 ± 0.01	4910.56 ± 1.97
	12	Blackish brown	Distinctive odour	Semisolid	5.40 ± 0.01	4812.96 ± 9.55
F3	0	Blackish brown	Distinctive odour	Semisolid	5.35 ± 0.005	3738.63 ± 0.40
	12	Blackish brown	Distinctive odour	Semisolid	5.16 ± 0.00	3666.76 ± 0.61
F4	0	Blackish brown	Distinctive odour	Semisolid	5.39 ± 0.00	3991.13 ± 0.64
	12	Blackish brown	Distinctive odour	Semisolid	5.20 ± 0.005	3858.66 ± 0.92

The stability evaluation of *Phyllanthus emblica* nanogel and gel formulations, focusing on organoleptic properties, pH, and viscosity, demonstrated consistent results over 12 weeks of storage at room temperature. The blank nanogel (F0) remained transparent, while formulations F1, F2, F3, and F4 maintained a stable blackish-brown color due to the extract, with no significant changes in odor or consistency, all retaining a distinctive odor and semisolid texture. This stability in appearance indicates good organoleptic resilience, crucial for product quality and consumer appeal. pH levels, important for compatibility with the skin's natural range (4.5-6.5), showed slight declines across all formulations; F0's pH dropped from 6.36 ± 0.01 to 6.18 ± 0.01, and F4's pH shifted from 5.39 ± 0.00 to 5.20 ± 0.005, while F1, F2, and F3 also experienced minimal decreases. Despite these slight changes, all pH values remained within safe limits, ensuring suitability for skin application without risk of irritation. Viscosity measurements, reflecting formulation consistency and ease of application, showed gradual declines across all samples: F0 reduced from 9738.46 ± 4.56 cP to 9572.16 ± 0.68 cP, and F4 decreased from 3991.13 ± 0.64 cP to 3858.66 ± 0.92 cP. Minor reductions were also observed in F1, F2, and F3, but all values remained within the optimal range (2000-50,000 cP), indicating consistent performance for practical application. Collectively, these findings confirm that *Phyllanthus emblica* nanogel and gel formulations exhibit excellent stability in terms of physical appearance, pH, and viscosity, making them well-suited for long-term storage and safe for topical use [21–23].

The cycling test, designed to assess stability under extreme temperature fluctuations, involved storing *Phyllanthus emblica* nanogel and gel formulations alternately at 4±2°C and 40±2°C for 24 hours each, constituting one cycle, and repeating this for six cycles to simulate seasonal or daily temperature changes. As shown in Table 8, all formulations (F0-F4) retained their physical and chemical integrity throughout the test. The organoleptic properties, including color, odor, and consistency, showed no significant alterations; F0 remained transparent, while F1, F2, F3, and F4 maintained a blackish-brown hue, a distinctive odor, and a semisolid consistency. pH levels decreased minimally and remained within the safe range for skin application, ensuring compatibility and reducing the risk of irritation. Additionally, viscosity measurements revealed only slight changes, indicating that the formulations maintained a stable, user-friendly consistency suitable for application. These findings confirm that the *Phyllanthus emblica* Nanogel and gel preparations exhibit robust thermal stability, underscoring their suitability for long-term storage and practical use.

Table (8): Cycling Test Results of Nanogel and gel Preparations.

Parameter	Formula	F0	F1	F2	F3	F4
Organoleptic	Color	Transparent	Blackish brown	Blackish brown	Blackish brown	Blackish brown
	Odor	Distinctive odour	Distinctive odour	Distinctive odour	Distinctive odour	Distinctive odour
	Consistency	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid
pH (Mean ± SD)	Before	6.36 ± 0.01	5.91 ± 0.01	5.58 ± 0.01	5.35 ± 0.005	5.39 ± 0.00
	After	6.35 ± 0.00	5.91 ± 0.02	5.57 ± 0.005	5.35 ± 0.005	5.39 ± 0.005
Viscosity (cP)	Before	9738.46 ± 4.56	6316.60 ± 10.09	4910.56 ± 1.97	3738.63 ± 0.40	3991.13 ± 0.64
	After	9738.07 ± 4.47	6316.23 ± 9.98	4910.03 ± 2.13	3738.46 ± 0.50	3990.83 ± 0.73

Antioxidant Activity Testing of Extract Nanogel and Gel Preparations

The antioxidant activity test results indicate that the *Phyllanthus emblica* fruit ethanol extract nanogel and gel formulations demonstrate IC_{50} values of 71.20 ± 0.22 µg/mL and 93.50 ± 0.30 µg/mL, respectively, as shown in Table 9. These values suggest that both the nanogel and gel formulations retain antioxidant activity, though they fall into a lower antioxidant category than the pure ethanol extract of *Phyllanthus emblica*, which has an IC_{50} value of 4.16 µg/mL. This indicates that the pure extract has a superior capacity to neutralize free radicals due to its higher concentration of bioactive compounds, such as phenolics and flavonoids, which contribute to potent antioxidant effects.

Table (9): Results of the Nanogel and gel Extract Antioxidant Activity Test.

Parameter	IC_{50} value (µg/mL)
Extract gel composition 7%	93.50±0.30
Extract Nanogel composition 7%	71.20±0.22

The decrease in antioxidant activity in the nanogel and gel formulations can be attributed to several factors. Primarily, the dilution of the extract during the formulation process reduces the concentration of active compounds. In topical formulations like gels and nanogels, extracts are often diluted to achieve optimal physical stability, viscosity, and user comfort. This reduction in active components, specifically flavonoids and phenolic compounds, results in lower antioxidant potency compared to the pure extract. Furthermore, the gel and nanogel matrices can influence the distribution and accessibility of antioxidant compounds, potentially limiting their interaction with free radicals [30,31].

The structure of gels and nanogels, semisolid preparations containing water and polymer, can affect the availability of active compounds to interact with free radicals. While the nanogel formulation demonstrated a slightly stronger antioxidant activity (IC_{50} 71.20 µg/mL) than the gel (IC_{50} 93.50 µg/mL), likely due to improved penetration and dispersion of active compounds within the nanogel matrix, both formulations provide antioxidant protection. Although their activity is less potent than that of the pure extract, the antioxidant capabilities of the gel and nanogel remain strong enough to protect against oxidative skin damage from UV exposure and environmental pollutants. These formulations are well-suited for use in cosmetic and skincare products, providing antioxidant benefits that help address oxidative stress-related skin issues, making them valuable for topical applications focused on skin health and protection [30,31].

Antibacterial Activity Testing of Extract Nanogel and Gel Preparations

This study evaluated and compared the antibacterial activity of *Phyllanthus emblica* fruit ethanol extract in both nanogel and gel formulations. The antibacterial efficacy was tested against *Propionibacterium acnes* and *Staphylococcus epidermidis*, with a negative control (gel without extract) to confirm that no other factors influenced the test results. Additionally, Clindamycin Phosphate 1% gel served as the positive control, as it is well-established for its strong antibacterial properties.

Table (10): Results of antibacterial activity testing of the extract gel.

Preparation	Diameter of inhibition area (mm; n=3)	
	***Propionibacterium acnes* ± SD**	***Staphylococcus epidermidis* ± SD**
Clindamycin Phosphate 1% (Control +)	26.28 ± 0.25	27.36 ± 0.66
F0	-	-
F1	10,70 ± 0,22	11,41 ± 0,76
F2	12,46 ± 0,35	14,10 ± 0,55
F3	15,33 ± 0,28	18,51 ± 0,57
F4	12,73 ± 0,68	15,54 ± 0,65

The antibacterial activity testing (Table 10) indicates that the *Phyllanthus emblica* fruit ethanol extract nanogel and gel formulations at 7% concentration demonstrate significant inhibitory effects against *Propionibacterium acnes* and *Staphylococcus epidermidis*. The positive control, Clindamycin Phosphate 1% gel, showed the highest inhibition zones, at 26.28 ± 0.25 mm against *P. acnes* and 27.36 ± 0.66 mm against *S. epidermidis*, highlighting its potent antibacterial properties. In comparison, the 7% nanogel formulation (F3) exhibited inhibition zones of 15.33 ± 0.28 mm for *P. acnes* and 18.51 ± 0.57 mm for *S. epidermidis*, while the 7% gel formulation (F4) showed zones of 12.73 ± 0.68 mm and 15.54 ± 0.65 mm, respectively. Although lower than those of Clindamycin, these values indicate strong antibacterial efficacy for both formulations [32,33].

The presence of antibacterial activity in both the nanogel and gel suggests that *Phyllanthus emblica* extract retains its effectiveness against acne-causing bacteria when formulated into these topical preparations. The nanogel showed slightly higher antibacterial activity than the gel, likely due to enhanced penetration and interaction with bacterial cells facilitated by the nanogel matrix. The negative control (F0), a base gel without extract, displayed no inhibition, confirming that the antibacterial effects stem from the active compounds in *Phyllanthus emblica*. Formulations with lower extract concentrations, F1 (3%) and F2 (5%), displayed moderate antibacterial activity, with inhibition zones of 10.70 ± 0.22 mm to 14.10 ± 0.55 mm, respectively, indicating a dose-dependent effect [32,33].

The strong antibacterial activity of the nanogel and gel can be attributed to the *Phyllanthus emblica* extract and the physicochemical properties of the formulations, which promote active compound delivery into bacterial cell walls, particularly in gram-positive bacteria such as *P. acnes* and *S. epidermidis*. Additionally, preservatives such as methyl and propyl parabens may enhance the formulation's antibacterial efficacy by disrupting bacterial membranes [32,33].

Statistical analysis, including the Shapiro-Wilk test and one-way ANOVA, confirmed significant differences in antibacterial activity across extract concentrations ($p<0.05$), with post hoc tests indicating significant differences ($p<0.001$) between the 7% gel formulation, the positive control, and the negative control. Although the nanogel and gel formulations exhibit slightly lower

inhibition zones than Clindamycin, they remain promising for topical antibacterial use in acne treatment, supported by their stability and effectiveness in managing bacterial infections associated with acne [32,33].

Skin Irritation Test

The skin irritation test was conducted using the nanogel formulation containing 7% *Phyllanthus emblica* fruit extract, representing the highest extract concentration applied in the formulation study. This approach was selected to ensure safety evaluation under the most conservative conditions. The irritation responses of six eligible volunteers are summarised in Table 11.

Table (11): Skin Irritation Test Results of *Phyllanthus emblica* Extract Nanogel (7%) on Human Volunteers.

Observation Parameter	Volunteer					
	1	2	3	4	5	6
Erythema (Redness)	–	–	–	–	–	–
Itching	–	–	–	–	–	–
Swelling	–	–	–	–	–	–

No signs of erythema, itching, or swelling were observed in any of the volunteers throughout the three-day observation period. All recorded parameters showed negative (–) responses, indicating the absence of visible skin irritation following repeated topical application of the nanogel formulation [34].

These findings indicate that the nanogel formulation was well tolerated on human skin under the conditions tested. The absence of irritation may be attributed to the biocompatible gel base and the controlled incorporation of the plant extract within the nanogel matrix, which may reduce direct contact of potentially irritant constituents with the skin surface. Although the present results support the formulation's preliminary dermal safety, further studies with a larger sample size and longer exposure duration are required to comprehensively confirm its long-term safety for topical use [34].

Conclusion

The *Phyllanthus emblica* fruit ethanol extract obtained by Microwave-Assisted Extraction demonstrated strong antioxidant and antibacterial properties, with phenolic and flavonoid compounds contributing significantly to its efficacy. Both the nanogel and gel formulations containing 7% extract showed promising potential for anti-acne applications, with the nanogel exhibiting slightly greater antibacterial activity against *Propionibacterium acnes* and *Staphylococcus epidermidis* than the gel. The physical and chemical stability of these formulations, maintained over 12 weeks, supports their suitability for topical use. These findings suggest that *Phyllanthus emblica* nanogel and gel formulations could serve as effective, natural alternatives for managing acne, offering antioxidant and antibacterial benefits.

Disclosure Statements

- Ethics approval and consent to participate: Not applicable
- **Consent for publication:** Not applicable
- **Author's contribution:** All authors contributed substantially to the completion of this research.
- **Availability of data and materials:** The raw data required to reproduce these findings are available in the body and illustrations of this manuscript.
- **Conflicts of interest:** The authors declare that there is no conflict of interest regarding the publication of this article.

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