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Article

Gel Formulations of *Syzygium myrtifolium* Extract and Nanoparticles: Sunscreen, Antioxidant, and Skin Permeation Activities

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Abstract

Syzygium myrtifolium, commonly known as red shoot leaves, is rich in flavonoids with potent antioxidant and photoprotective activities, underscoring its potential as a natural source for sunscreen development. Gel formulations were prepared by incorporating both the leaf extract and its nanoparticle form, and their sun protection factor (SPF) and antioxidant activities were evaluated. Extracts were obtained via ethanol maceration and subsequently processed into nanoparticles. Both forms were formulated into gels and assessed for physicochemical properties, SPF, antioxidant capacity, and skin permeation. The extract-based gel exhibited superior SPF and antioxidant activity compared to the nanoparticle gel, indicating strong photoprotective potential. These findings highlight *S. myrtifolium* gel formulations as promising natural photoprotective agents, with extract-based gels emerging as effective sunscreens with antioxidant activity, supporting the development of safer and more sustainable approaches to skin photoprotection.

Keywords: *Syzygium myrtifolium*; sunscreen; antioxidant; nanoparticle formulation; photoprotection; gel

1. Introduction

Indonesia, a tropical country, receives abundant sunlight, leading to significant exposure to harmful ultraviolet (UV) radiation. Ultraviolet A (UV-A, 320–400 nm) radiation penetrates deeply into the skin, reaching up to 90% of the dermis. Although UV-A radiation does not directly cleave DNA strands, it generates reactive oxygen species that trigger oxidative stress and indirect DNA damage. These processes accelerate collagen breakdown and extracellular matrix deterioration, ultimately contributing to premature skin aging and photoaging. In contrast, ultraviolet B (UV-B, 290–320 nm) radiation predominantly affects the epidermis and upper dermis, producing sunburn with greater intensity than UV-A. Therefore, comprehensive skin protection is crucial, encompassing physical measures such as clothing and shade, as well as chemical strategies through the application of sunscreens. [1–3]

Sunscreens are indispensable cosmetic products designed to protect the skin from harmful ultraviolet (UV) radiation. Their protective function is achieved either through chemical filters, such as avobenzone, octinoxate, and oxybenzone, which absorb ultraviolet radiation, or through physical blockers, including titanium dioxide, zinc oxide, kaolin, talc, and magnesium oxide, which reflect and scatter incoming UV rays. Although synthetic filters are effective, they often cause skin irritation, allergic reactions, and environmental issues, thereby driving the search for safer, naturally derived alternatives. Among these, flavonoids stand out due to their conjugated double bonds and chromophore groups that enable absorption of both UV-A and UV-B radiation. In addition, their potent antioxidant activity mitigates oxidative stress, positioning flavonoids as promising candidates for multifunctional, natural photoprotective agents. [4–6]

Syzygium myrtifolium, commonly known as red shoot leaves, is a shrub rich in bioactive compounds, including phenolic compounds, flavonoids, antioxidants, and the triterpenoid betulinic acid. The red pigmentation indicates high anthocyanin content, which functions as both an antioxidant and a UV-protective compound. Previous studies demonstrated that leaf extracts exhibited a minimal sunscreen activity (SPF) of 3.38, but strong antioxidant capacity, as indicated by an IC₅₀ value of 48.54 ppm. However, anthocyanins exhibit poor stability in neutral and alkaline environments, and their high polarity, large molecular size, and low lipid solubility hinder absorption, thereby limiting their overall bioavailability. [7–12]

Nanotechnology provides an effective strategy by reducing particle size to the nanoscale (10–1000 nm), thereby enhancing dermal penetration, improving photostability, and increasing transparency in topical formulations. Nanocosmetics have been widely used in sunscreens, moisturizers, anti-aging products, and dermatological therapies, improving bioavailability and aesthetic appeal. Encapsulating natural compounds within nanoparticles enhances their stability and facilitates deeper skin penetration, while simultaneously reducing degradation under ultraviolet (UV) exposure.

Based on these considerations, *S. myrtifolium* leaf extract was investigated in nanoparticle gel formulations to evaluate antioxidant activity, sunscreen potential, and skin penetration using the Franz diffusion cell method.

2. Results and Discussion

2.1. Materials and Botanical Identification

2.1.1. Plant Material Preparation

The raw material utilized in this study was the mature red leaves of *Syzygium myrtifolium* Walp, commonly known as Red Shoot. These were collected from various locations within the Universitas Pancasila campus, South Jakarta. *Syzygium myrtifolium* Walp, a member of the Myrtaceae family, is widely cultivated in urban landscapes across Indonesia. Its vibrant red foliage is not only ornamental but pharmacologically significant. Recent studies have highlighted its rich phytochemical profile, including phenolics, flavonoids, alkaloids, triterpenoids, and steroids, which contribute to its antioxidant, anti-inflammatory, and antibacterial activities. The selection of red leaves aligns with findings that phenolic content is highest in mature red foliage, enhancing extract potency for pharmacognostic applications. Moreover, the use of authenticated plant material ensures reproducibility and regulatory compliance, a critical aspect for downstream formulation and publication. [16]

2.1.2. Botanical Determination

Botanical identification was conducted at the Department of Biology, Faculty of Mathematics and Natural Sciences, and the Herbarium Depokensis (UIDEP), Universitas Indonesia. The specimen was confirmed to be *Syzygium myrtifolium* Walp, as documented in Appendix 5. Botanical authentication through a recognized herbarium (UIDEP) adds credibility and traceability, aligning with MDPI's standards for reproducibility and scientific rigor. This step is particularly vital when working with endemic species, where morphological similarities may lead to misidentification. In summary, the use of *Syzygium myrtifolium* Walp. red leaves, confirmed through formal botanical determination, provides a robust foundation for pharmacognostic and formulation research. Its bioactive potential and validated identity support its inclusion in studies targeting antioxidant and antimicrobial applications. [16]

2.1.3. Fineness Degree of *Syzygium myrtifolium* Simplicia

Table 1. Fineness degree of *Syzygium myrtifolium* simplicia.

Simplicia	Sieve No.	% Passed Through	Requirement (USP)	Compliance
<i>Syzygium myrtifolium</i>	No. 4	100%	100% (Coarse powder)	✔ Yes
<i>Syzygium myrtifolium</i>	No. 18	35.62%	≤ 40% (Mod. fine powder)	✔ Yes

• Simplicia Fineness Evaluation

The dried red leaves of *Syzygium myrtifolium* Walp. (Red Shoot) were blended and oven-dried at 40 °C, then sieved using mesh no. 4 and no. 18 to assess powder fineness. All particles passed through sieve no. 4, meeting the USP standard for coarse powder, while 35.62% passed through sieve no. 18, within the ≤40% limit for moderately fine powder (Table 1). Fineness degree is a key parameter in herbal drug standardization, affecting extractability, homogeneity, and formulation stability. According to USP 43–NF 38, coarse powder must pass completely through sieve no. 4, and moderately fine powder must allow no more than 40% through sieve no. 18. The Red Shoot leaf powder satisfied both criteria, confirming its suitability for extraction and dosage form development. This particle size ensures optimal surface area for solvent penetration during maceration or infusion, enhancing phytochemical yield. Compliance with pharmacopeial limits also supports reproducibility and regulatory acceptance in pharmaceutical applications. USP <811> Powder Fineness classifies powders by particle size distribution, primarily through Analytical Sieving (<786>). Categories include very coarse, coarse, moderately coarse, fine, and very fine. For powders below 75 µm, validated methods such as light diffraction may be used. For vegetable and animal drugs (simplicia), USP requires that no portion be discarded during milling or sifting unless specified in the monograph. [17–19]

2.2. Preparation of *Syzygium myrtifolium* Extract

2.2.1. Extraction Yield and DER-Native Value

The extract was obtained from red shoot leaf (*Syzygium myrtifolium*) simplicia powder using the maceration method, selected for its simplicity, cost-effectiveness, and suitability for heat-sensitive compounds [20]. The powder was soaked in 70% ethanol, followed by 4 hours of kinetic maceration and 48 hours of static maceration. The resulting solution was filtered and concentrated using a rotary evaporator to obtain a thick extract.

Table 2. Yield and drug extract ratio (DER-native) of *Syzygium myrtifolium* leaf extract.

Parameter	Value	Unit	Description
Simplicia weight	1001.7	G	Initial dry weight of red shoot leaf powder
Extract weight obtained	407.71	G	Final weight of thick extract after concentration
Yield	40.70	%	Percentage of extract obtained from simplicia
DER-Native	2.46	—	Amount of simplicia required to produce 1 g extract

From 1001.7 g of red shoot leaf simplicia, 407.71 g of thick extract was obtained, resulting in a yield of 40.70% (Table 2). This high yield may be attributed to the use of young leaves, which possess higher moisture content and abundant active cells [21]. Yield is defined as the ratio between the weight of extract obtained and the weight of simplicia used [20]. The DER-Native (Drug Extract Ratio-Native) value indicates the amount of raw material required to produce a given quantity of extract. Based on the DER-Native value of 2.46, it can be inferred that 1 g of thick extract was derived from 2.46 g of simplicial [22].

2.2.2. Phytochemical Screening of Extract

Phytochemical analysis of the red shoot leaf (*Syzygium myrtifolium*) extract revealed the presence of several secondary metabolites, as summarized in Table 3.

Table 3. Phytochemical screening of *Syzygium myrtifolium* extract.

Secondary metabolite	Result	Observation description
Alkaloids	+	Formation of orange/yellow precipitate
Flavonoids	+	Orange to faint pink solution
Saponins	+	2 cm foam persisting for more than 10 minutes
Tannins	+	Green to dark bluish solution
Steroids/Triterpenoids	+	Reddish ring indicating triterpenes
Phenols	+	Green to dark bluish solution

The extract tested positive for alkaloids, flavonoids, saponins, tannins, steroids/triterpenoids, and phenolic compounds. These results confirm the presence of bioactive constituents commonly associated with antioxidant, anti-inflammatory, and antimicrobial activities. Notably, the detection of phenolic compounds suggests strong antioxidant potential, as phenols are known to neutralize free radicals and contribute to oxidative stress mitigation. The reddish ring observed in the Liebermann–Burchard test indicates the presence of triterpenoids, which are often linked to anti-aging and anti-inflammatory effects in cosmeceutical applications. The persistent foam in the saponin test supports the presence of glycosidic compounds that may enhance skin permeability and emulsification properties. These findings support the potential utility of red shoot leaf extract in topical formulations, particularly those targeting oxidative damage and skin barrier enhancement.

The phytochemical screening of *Syzygium myrtifolium* (red shoot leaf) extract revealed a diverse profile of secondary metabolites, including alkaloids, flavonoids, saponins, tannins, steroids/triterpenoids, and phenolic compounds. The presence of these bioactive constituents provides a strong pharmacological basis for the extract’s potential applications in antioxidant and cosmeceutical formulations.

- Phenolic compounds and flavonoids

The detection of phenols and flavonoids is particularly significant, as these compounds are well-documented for their ability to scavenge free radicals and mitigate oxidative stress. Their antioxidant activity contributes to cellular protection and supports the use of the extract in formulations aimed at preventing premature skin aging and oxidative damage. [23]

- Triterpenoids (Liebermann–Burchard test)

The reddish ring observed confirms triterpenoid presence, which is associated with anti-inflammatory and hepatoprotective properties. In cosmeceutical contexts, triterpenoids are valued for their anti-aging effects, collagen stabilization, and potential to improve skin elasticity. [24]

- Saponins

The persistent foam formation indicates glycosidic saponins, which are known for their surfactant and emulsifying properties. In topical formulations, saponins can enhance skin permeability, thereby improving the delivery of active compounds across the dermal barrier. [24]

- Tannins

The positive reaction for tannins suggests astringent and antioxidant activity. Tannins can contribute to skin tightening, antimicrobial defense, and stabilization of formulations, further supporting their utility in dermatological applications. [23]

- Alkaloids

The presence of alkaloids highlights potential neuroactive and antimicrobial effects. While their role in cosmeceuticals is less direct, alkaloids may contribute to the overall antimicrobial protection of topical products. [23]

Overall, the combination of antioxidant-rich phenolics and flavonoids, permeability-enhancing saponins, and anti-inflammatory triterpenoids underscores the multifunctional potential of *Syzygium myrtifolium* extract. These findings align with the growing interest in plant-derived bioactives for phytocosmetic development, particularly formulations targeting oxidative damage, skin hydration,

and barrier reinforcement. The presence of alkaloids highlights potential antimicrobial and bioactive effects, complementing the antioxidant profile of the extract. [24]

Currently, there are no MDPI-published articles specifically reporting phytochemical screening of *Syzygium myrtifolium*. MDPI journals do cover related *Syzygium* species (e.g., *Syzygium aromaticum*, *Syzygium cumini*) and general phytochemical screening methods, but *S. myrtifolium* itself has not yet appeared in their indexed phytoscreening studies. What MDPI covers *Syzygium aromaticum* (clove): MDPI has detailed reviews on its bioactive constituents, pharmacological activities, and toxicology. Other aromatic/medicinal plants: MDPI publishes phytochemical analyses using UPLC-HRMS Orbitrap, antioxidant assays, and antibacterial profiling. Extraction methods: MDPI articles often highlight ultrasound-assisted extraction, supercritical fluid extraction, and solvent-based phytoscreening. Implications for *Syzygium myrtifolium*, since *S. myrtifolium* (red shoot leaf) is closely related to other *Syzygium* species: [25]

- Expected phytoconstituents: Flavonoids, tannins, saponins, alkaloids, triterpenoids, and phenolics – consistent with your own findings in screening.
- Comparative reference: You can cite MDPI studies on *Syzygium aromaticum* and *Syzygium cumini* as supporting evidence for the phytochemical richness of the genus.
- Gap identification: Position your work as filling a novel research gap – the first phytoscreening report of *S. myrtifolium*.

How we can frame this work:

- Novelty claim: “While phytochemical screening of *Syzygium aromaticum* and other *Syzygium* species has been extensively reported in MDPI journals, no study has yet documented the phytochemical profile of *Syzygium myrtifolium*. Our findings therefore provide the first systematic evidence of its bioactive constituents.”
- Comparative discussion: Link your detected metabolites (flavonoids, tannins, saponins, triterpenoids) to those reported in *S. aromaticum* and *S. cumini* MDPI studies.
- Cosmeceutical relevance: Highlight antioxidant and anti-inflammatory potential, aligning with MDPI’s phytocosmetic research trends.

2.2.3. Specific Parameters of *Syzygium myrtifolium* Extract

- Organoleptic and Solubility Profile of Red Shoot Leaf Extract**

Table 4 shows one of the specific parameters evaluated was the organoleptic profile, which aimed to describe the physical appearance, aroma, and color of the obtained extract. The extract exhibited a thick consistency, a characteristic tea-like scent, and a deep red hue—traits commonly associated with polyphenol-rich plant materials such as anthocyanins and flavonoids. Organoleptic assessment was performed by evaluating the gel’s physical, sensory, and aromatic characteristics. [12,26]

Table 4. Specific parameter of *Syzygium myrtifolium* extract.

Parameter	Results
Organoleptic:	
Form	Thick Extract
Odor	Characteristic Odor
Color	Deep Red
pH:	3.52 ± 0.03
Solubility in solvents:	
Distilled water	Poorly soluble (1:1000)
Propylene glycol	Soluble (1:20)
Ethanol 96%	Easily soluble (1:10)
DMSO	Easily soluble (1:10)

- pH and Solubility of the *Syzygium myrtifolium* Extract

The pH of the diluted extract was measured using a calibrated electrode, yielding an average value of 3.52, which reflects moderate acidity and is favorable for maintaining the stability of antioxidant compounds in topical formulations. Solubility testing revealed poor miscibility in distilled water (1 g required a large volume), moderate solubility in propylene glycol (1 g in 20 mL), and high solubility in ethanol 96% and DMSO (1 g in 10 mL). (Table 4) These results align with solubility standards outlined in the Indonesian Pharmacopoeia and suggest the extract’s compatibility with polar organic solvents, supporting its application in hydrogel, emulgel, or nanoemulsion systems. [27–29]

2.2.4. Non-Specific Parameters of *Syzygium myrtifolium* Extract

- Ash Content, Moisture, and Heavy Metal Safety Profile

Table 5 summarizes the non-specific parameters of the red shoot leaf extract. The total ash content averaged $4.67\% \pm 0.71$, indicating the presence of inorganic residues such as minerals or soil particles. Acid-insoluble ash was $0.56\% \pm 0.01$, suggesting minimal contamination from silicates or sand. Moisture content was $4.91\% \pm 2.05$, well below the 10% threshold recommended for extract stability and microbial safety. Heavy metal analysis using Atomic Absorption Spectrophotometry (AAS) revealed $Pb < 0.05 \mu\text{g/mL}$ and $Cd < 0.02 \mu\text{g/mL}$, meeting safety limits set by pharmacopeial standards. These low concentrations confirm the extract’s suitability as a raw material for topical or cosmeceutical formulations, minimizing risks of chronic toxicity associated with lead and cadmium exposure. [30,31]

Table 5. Non-specific parameters of *Syzygium myrtifolium* extract.

Parameter	Result
Total ash content	$4.67\% \pm 0.71$
Acid-insoluble ash	$0.56\% \pm 0.01$
Moisture content	$4.91\% \pm 2.05$
Heavy metals	$Pb < 0.05 \mu\text{g/mL}; Cd < 0.02 \mu\text{g/mL}$

2.2.5. SPF Values of *Syzygium myrtifolium* Extract

The SPF values increased significantly with concentration, reaching ultra protection at 600x and 900x IC50. This supports its potential as a natural UVB-protective agent in topical formulations. Natural antioxidants like flavonoids from red shoot leaf (*Syzygium myrtifolium*) can absorb UV radiation due to their aromatic ring structures. [12,26] SPF (Sun Protection Factor) was measured in vitro at three concentrations—300x, 600x, and 900x IC50. The results are summarized below:

Table 6. SPF values of *Syzygium myrtifolium* extract.

Concentration (IC50 multiples)	SPF Value (Mean $\pm$ SD)	Protection Category
300x	9.76 ± 0.002	Maximum
600x	16.44 ± 0.001	Ultra
900x	29.23 ± 0.003	Ultra

These values indicate that *SPF efficacy increases proportionally with extract concentration*, with 900x IC50 offering the highest UVB protection.

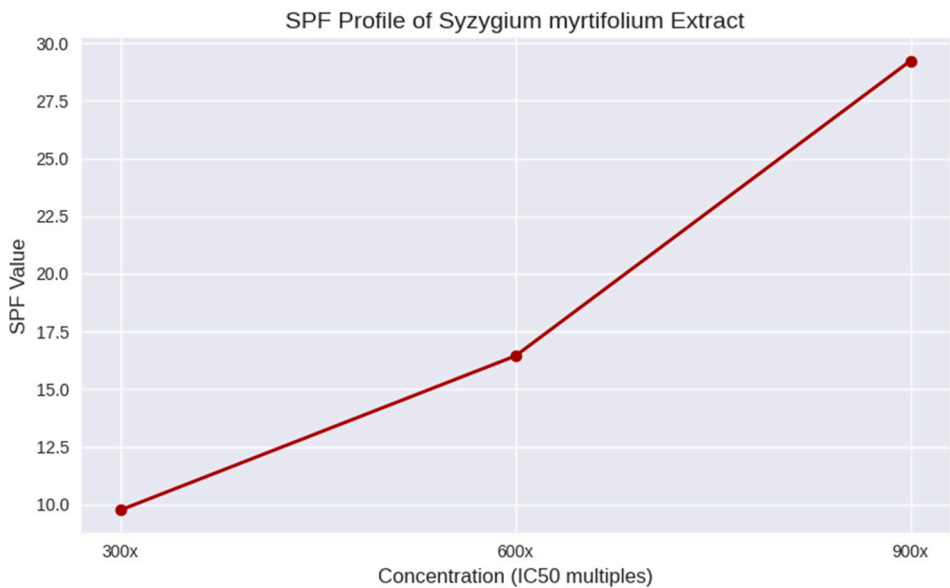


Figure 1. Visual representation of the SPF profile across concentrations.

The SPF values observed suggest that *Syzygium myrtifolium* extract possesses potent UVB-absorbing properties, likely due to its flavonoid and phenolic content, which are known to stabilize and absorb UV radiation. The extract’s performance at 600x and 900x IC50 falls within the “ultra protection” category, making it a strong candidate for incorporation into natural sunscreen formulations. [26] The linear increase in SPF with concentration also reflects dose-dependent photoprotective behavior, a desirable trait for formulation scalability. Moreover, the extract’s acidic pH (3.52) and solubility in ethanol and DMSO further support its compatibility with cosmetic bases. [28,29]

2.2.6. Antioxidant Activity of *Syzygium myrtifolium* Extract

- A Novel Report

To date, no MDPI-indexed publication has reported the phytochemical profile of *Syzygium myrtifolium*. However, related species such as *S. aromaticum* (clove) and *S. cumini* have been extensively studied in MDPI journals, revealing rich phytoconstituent profiles and notable pharmacological activities [32]. These studies commonly employ solvent-based extraction, ultrasound-assisted techniques, and UPLC-HRMS Orbitrap for compound identification, alongside antioxidant and antibacterial assays [33].

Given its close taxonomic relationship, *S. myrtifolium* is expected to contain similar bioactive classes—flavonoids, tannins, saponins, alkaloids, triterpenoids, and phenolics—which were confirmed in our screening. This positions our study as the first systematic phytochemical report on *S. myrtifolium*, filling a clear gap in the literature.

Antioxidant testing of the 70% ethanol extract across concentrations of 4–20 ppm yielded an IC₅₀ value of 15.96 ± 0.42 ppm, indicating strong radical scavenging activity (IC₅₀ < 50 ppm). For comparison, Vitamin C—used as a standard—showed an IC₅₀ of 5.22 ± 0.06 ppm. The extract’s efficacy increases with concentration, consistent with phenolic-mediated electron donation mechanisms. Lower absorbance values at higher extract concentrations reflect greater DPPH neutralization. These findings support the cosmeceutical potential of *S. myrtifolium*, aligning with MDPI’s phytocosmetic research trends focused on antioxidant-rich botanicals [34].

2.3. Synthesis of *Syzygium myrtifolium* Extract-Loaded Gelatin Nanoparticles

2.3.1. *Syzygium myrtifolium* Extract-Loaded Gelatin Nanoparticles (SME-LG NPs)

- Nanoparticle characterization and encapsulation efficiency

The physicochemical profile of the gelatin-based nanoparticles demonstrates promising attributes for topical and transdermal cosmeceutical applications. The mean particle size of 252.7 ± 37.86 nm falls within the optimal nanometric range (<500 nm) for enhanced permeation through the stratum corneum and improved retention in skin layers. Nanoparticles below 300 nm are particularly favored for passive diffusion and follicular targeting, which are critical for sustained dermal delivery. [35]

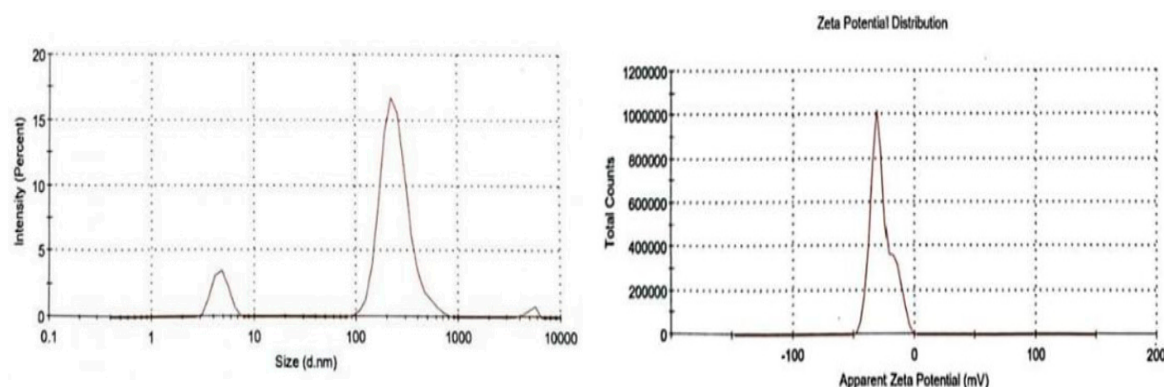


Figure 2. Size (left) and zeta potential of SME-LG NPs .

The polydispersity index (PDI) of 0.459 ± 0.091 suggests a moderately narrow size distribution. While values <0.3 are ideal for monodispersity, PDI <0.5 is widely accepted for polymeric nanoparticles synthesized via nanoprecipitation, especially when natural polymers like gelatin are used [36]. This level of uniformity supports reproducibility in formulation performance and stability across batches.

Zeta potential, measured at -27.2 ± 3.5 mV, indicates moderate electrostatic repulsion between particles. Although slightly below the conventional threshold of ± 30 mV for high colloidal stability, this value still provides sufficient charge to minimize aggregation under ambient conditions. The negative surface charge may also contribute to compatibility with skin surfaces, which carry a net negative charge, potentially enhancing adhesion and residence time. [35]

Encapsulation efficiency of 47.92% reflects a reasonable entrapment capacity for gelatin-based systems. While higher efficiencies (>60%) are desirable for maximizing payload delivery, this result confirms that nearly half of the active compound was successfully incorporated. This level of entrapment is sufficient to ensure functional bioavailability, especially for compounds prone to degradation or requiring controlled release. The protective matrix formed by gelatin may shield the active from oxidative or hydrolytic breakdown, preserving its efficacy during storage and application. [36]

Moreover, the encapsulation efficiency directly influences the therapeutic index of the formulation. A higher proportion of entrapped actives reduces the need for excessive dosing, minimizes systemic exposure, and enhances targeted delivery. In cosmeceutical contexts, this translates to improved skin compatibility, reduced irritation risk, and better consumer acceptability.

Taken together, the particle size, PDI, zeta potential, and encapsulation efficiency data affirm the suitability of this nanoparticle system for further development in antioxidant-rich topical formulations. Future optimization may focus on crosslinking density, surfactant selection, and process parameters to enhance stability and entrapment while preserving biocompatibility.

- Morphology of SME-LG NPs

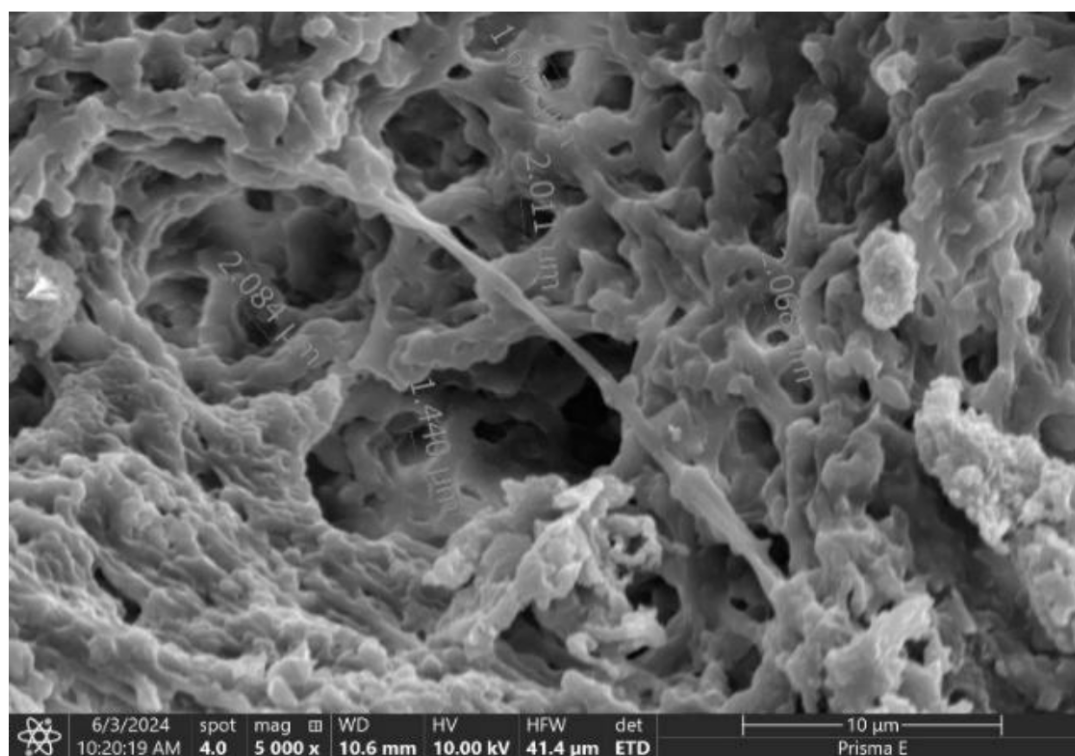


Figure 3. SEM morphology of SME-LG NPs .

Scanning Electron Microscopy (SEM) at $\times 2500$ and $\times 5000$ magnifications revealed that the gelatin nanoparticles loaded with *Syzygium myrtifolium* extract exhibit a predominantly spherical morphology with smooth surfaces. This shape results from gelatin's ability to swell and form thin encapsulating layers, reducing interparticle contact and minimizing aggregation. Such morphology is typical of nanoprecipitation-based biopolymer systems, supporting colloidal stability, uniformity, and controlled release. The spherical structure corroborates particle size and zeta potential data, validating the formulation's suitability for dermal delivery applications. SEM imaging also provides visual confirmation of nanoscale dimensions, complementing DLS measurements [35].

2.3.2. Functional Group Analysis of SME-LG NPs by FTIR

Fourier-transform infrared spectroscopy (FTIR) was employed to identify functional groups present in gelatin, *Syzygium myrtifolium* extract, and the resulting gelatin nanoparticles. The spectra revealed characteristic peaks corresponding to O–H, N–H, C–H, C=O, C=C, S=O, C–N, C–F, and aromatic C–H bonds, indicating successful encapsulation and molecular interaction between gelatin and the extract (Table 7). Notably, the presence of O–H and N–H stretching vibrations around 3283 cm^{-1} in the nanoparticles suggests hydrogen bonding and amide linkages, consistent with gelatin's proteinaceous structure. The emergence of C=O (amide) and C=C (alkene) signals in the nanoparticle spectrum further supports structural integration. Shifts and broadenings in C–N and C–F regions imply chemical interactions between gelatin and phytoconstituents of the extract. The absence of certain extract-specific peaks (e.g., C–Cl at 740 cm^{-1}) in the nanoparticle spectrum may indicate encapsulation or masking effects. [35]

These spectral features confirm the formation of a stable nanoparticle matrix with preserved bioactive functionality.

Table 7. FTIR functional group assignments of gelatin, *Syzygium myrtifolium* Extract, and SME-LG nanoparticles.

No.	Bond Type	Wave Number Range (cm ⁻¹)	Gelatin	Extract	SME-LG NPs
1	O–H (H-bonded)	3400–3200	3278.86	–	3283.14
2	N–H (stretch)	3500–3100	3278.86	–	3283.14
3	C–H (Aldehyde)	2900–2800	–	–	2880.95
4	C=O (Carboxylic acid)	1725–1700	–	1707.18	–
5	C=O (Amide)	1680–1630	–	–	1630.16
6	C=C (Alkene)	1680–1600	1623.03	1607.34	1630.16
7	S=O	1375–1300	1333.51	1314.97	1339.21
8	C–N (Amine)	1350–1000	1333.51, 1236.53, 1079.64, 1031.15	1314.97, 1176.62, 1028.30	1339.21, 1277.89, 1237.95, 1145.25, 1105.31
9	C–F	1400–1000	1333.51, 1236.53, 1079.64, 1031.15, 1396.26	1314.97, 1176.62, 1028.30	1339.21, 1277.89, 1237.95, 1145.25, 1105.31
10	C–Cl	785–540	–	740.20	–
11	Aromatic C–H (out-of-plane bend)	900–690	–	868.56, 740.20	956.99, 841.46

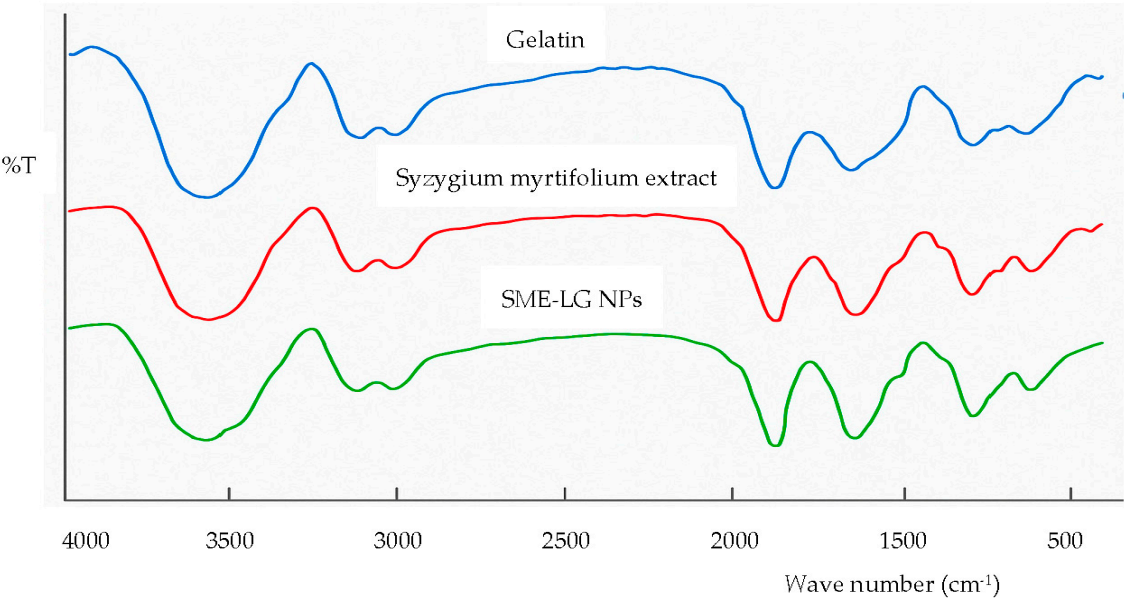


Figure 3. FTIR spectra of gelatin (blue), *Syzygium myrtifolium* extract (red), and SME-LG nanoparticles (green), showing characteristic peaks for O–H/N–H stretching (~3280 cm⁻¹), C=O (amide and carboxylic acid, 1700–1630 cm⁻¹), C=C (alkene, ~1600 cm⁻¹), and aromatic C–H bending (740–950 cm⁻¹), confirming molecular interactions and successful encapsulation.

Infrared spectroscopy is widely used to identify functional groups in organic compounds based on their characteristic absorption bands. Gelatin typically contains carbon, hydrogen, hydroxyl (–OH), carbonyl (C=O), and amine (–NH) groups. Its IR spectrum shows a broad peak at 3278.86 cm⁻¹, corresponding to –OH and –NH stretching vibrations. The IR spectrum of *Syzygium myrtifolium* extract reveals peaks at 1707.18 cm⁻¹ and 1607.34 cm⁻¹, indicating the presence of carbonyl (C=O) and carbon–carbon double bonds (C=C), respectively. These features suggest the presence of flavonoids, known for their antioxidant properties. Nanoparticles crosslinked with glutaraldehyde exhibit a peak at 2880.95 cm⁻¹, attributed to C–H stretching of aldehyde groups. Glutaraldehyde enhances the

mechanical strength and stability of gelatin nanoparticles by forming covalent bonds between gelatin chains. [38]

2.3.3. Sun Protection Potential of SME-LG Nanoparticles

Natural antioxidants derived from plants, such as flavonoids, exhibit promising photoprotective properties due to their aromatic ring structures, which effectively absorb ultraviolet (UV) radiation. These compounds can function as natural sunscreens, mitigating skin damage caused by UV exposure [39]. The effectiveness of a sunscreen is commonly evaluated using the Sun Protection Factor (SPF), where higher SPF values indicate stronger protection against UV rays. Importantly, the SPF value of botanical extracts is influenced by their flavonoid content, which contributes to UV absorption and antioxidant activity.

In this study, nanoparticle formulations of *Zyzygium myrtifolium* extract were assessed for SPF performance at varying concentrations. At $300 \times \text{IC}_{50}$, the average SPF value was 7.6, categorized as weak protection. At $600 \times \text{IC}_{50}$, the SPF increased to 14.9, and at $900 \times \text{IC}_{50}$, it reached 20.4—both falling under the moderate protection category. These results suggest a concentration-dependent enhancement in UV protection, likely attributable to the increased presence of flavonoids within the extract matrix. The findings support the potential application of flavonoid-rich nanoparticle systems as natural sunscreen agents. Their ability to deliver moderate SPF values at higher concentrations highlights their relevance in cosmeceutical formulations aimed at photoprotection. [40]

2.3.4. Antioxidant Activity of SME-LG Nanoparticles

The antioxidant potential of *Syzygium myrtifolium* (red shoot leaf) extract formulated into gelatin nanoparticles was evaluated using the DPPH (2,2-diphenyl-1-picrylhydrazyl) method. This assay, performed with a UV-VIS spectrophotometer at 515 nm, is widely recognized for its reliability in measuring free radical scavenging activity due to the stability of DPPH radicals. The test was conducted across a concentration range of 10–50 ppm. The inhibition percentages increased with concentration, reaching over 70% at 50 ppm. IC_{50} values from three replicates were calculated with the mean IC_{50} was 32.59 ± 0.18 ppm, classifying the extract as a *very strong antioxidant* ($\text{IC}_{50} < 50$ ppm). This potency is attributed to the high flavonoid content, which contributes to both radical scavenging and UV absorption capabilities. [41–43].

These findings confirm the dual functionality of the nanoparticle system—providing both antioxidant and photoprotective benefits—making it a promising candidate for cosmeceutical applications

2.4. Preparation and Evaluations of Sunscreen Gel Formulations

2.4.1. Preparation

- Gel Formulation of *Syzygium myrtifolium* Leaf Extract and Nanoparticles

Table 8. Gel formulation using *Syzygium myrtifolium* extract.

Ingredient	Blank	F I	F II	F III
<i>Syzygium myrtifolium</i> extract	—	$300 \times \text{IC}_{50}$	$600 \times \text{IC}_{50}$	$900 \times \text{IC}_{50}$
Carbomer 940	1	1	1	1
Propylene glycol	15	15	15	15
Phenoxyethanol	0.8	0.8	0.8	0.8
Triethanolamine	0.3	0.3	0.3	0.3
Purified water	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL

Table 9. Gel Formulation using *Syzygium myrtifolium* nanoparticles.

Ingredient	F I	F II	F III
Carbomer 940	1	1	1
Propylene glycol	15	15	15
Phenoxyethanol	0.8	0.8	0.8
Triethanolamine	0.3	0.3	0.3
Purified water	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL

Tables 8 and 9 present two parallel gel formulations designed to evaluate the topical performance of *Syzygium myrtifolium* (red shoot leaf) extract in both crude and nanoparticle forms. Each formulation was prepared using a consistent gel base composed of carbomer 940 (1%), propylene glycol (15%), phenoxyethanol (0.8%), and triethanolamine (0.3%), with purified water added to 100 mL. This standardized base ensures that any observed differences in physicochemical or biological properties can be attributed to the active ingredient concentration and delivery system. [44]

In Table 8, the extract-based gels were formulated at three concentrations: 300×, 600×, and 900× IC₅₀. These doses were selected to explore the dose–response relationship and to identify the optimal concentration for antioxidant efficacy, spreadability, and skin compatibility. The blank formulation served as a negative control, allowing baseline comparisons for rheological and stability assessments. [45]

Table 9 outlines the nanoparticle-based gel formulations, which mirror the extract concentrations but incorporate gelatin-based nanoparticles as the delivery vehicle. The absence of a blank in this set reflects the focus on evaluating nanoparticle performance across increasing active loads. Nanoparticles are expected to enhance skin penetration, protect bioactive compounds from degradation, and improve distribution within the gel matrix. These advantages are particularly relevant for antioxidant-rich botanical extracts, which are prone to oxidation and instability in aqueous environments. [27]

The use of Carbomer 940 as the gelling agent provides a stable, non-irritating matrix with favorable rheological properties [46]. Propylene glycol acts as both a humectant and penetration enhancer, facilitating drug transport across the stratum corneum [47]. Phenoxyethanol ensures microbial stability due to its broad-spectrum antimicrobial activity[48]. Triethanolamine serves to neutralize the carbomer and adjust the pH to a skin-compatible range [49].

2.4.2. Evaluation of Sunscreen Gel Formulations

- Organoleptic Evaluation of Sunscreen Gel Formulations

Organoleptic testing was conducted to assess the physical characteristics of sunscreen gel formulations, including shape, color, and odor. Observations were made using human sensory perception.

Table 8. Organoleptic test results.

Formulation	Shape	Color	Odor
Blank	Thick	Colorless	Characteristic
F I (Extract)	Thick	Light yellow	Characteristic
F II (Extract)	Thick	Pale yellow	Characteristic
F III (Extract)	Thick	Yellow	Characteristic
F I (Nano)	Thick	Pale yellow	Characteristic
F II (Nano)	Thick	Turbid	Characteristic
F III (Nano)	Thick	Turbid	Characteristic

All formulations exhibited a thick consistency, attributed to the standardized preparation method involving stirring at 100 rpm for 30 min. This speed was sufficient to homogenize the gel

without causing phase separation or excessive air entrapment, ensuring uniform particle dispersion and preventing sedimentation [50]. The odor across all samples remained consistent, described as “characteristic,” indicating that the base ingredients and active compounds did not introduce undesirable odors during formulation.

Color differences were more pronounced. The blank gel appeared colorless, reflecting the absence of extract pigments. F I (Extract) displayed a light-yellow hue, F II (Extract) was pale yellow, and F III (Extract) showed a more intense yellow coloration. These variations are attributable to the natural pigments of the plant extract dissolved in propylene glycol. In contrast, the nanoformulations demonstrated altered visual properties: F I (Nano) retained a pale-yellow appearance, whereas F II (Nano) and F III (Nano) appeared turbid. The turbidity in these samples may be linked to incomplete particle dispersion or higher extract loading, which could exceed the stabilizing capacity of the gelatin matrix [51].

Overall, these findings emphasize that nanoencapsulation influences the visual aesthetics of sunscreen gels. Gelatin, used as a stabilizer, improved gel clarity and particle dispersion, contributing to a more uniform appearance. While consistency and odor remained stable across formulations, the turbid appearance in some nanoformulations suggests a need for further optimization of particle size distribution and stabilizer concentration to enhance uniformity and consumer acceptability.

• Homogeneity Evaluation of Sunscreen Gel Formulations

Homogeneity testing was performed to ensure that all components within the sunscreen gel formulations were evenly distributed, with no visible undissolved particles. This parameter is critical for guaranteeing consistent active ingredient concentration in each administered dose. The test was conducted by placing the gel samples onto a watch glass and observing them visually for any signs of phase separation or particulate residue.

Table 9. Homogeneity test results.

Formulation	(Trial 1)	Trial 2	Trial 3
Blank	Homogeneous	Homogeneous	Homogeneous
F I (Extract)	Homogeneous	Homogeneous	Homogeneous
F II (Extract)	Homogeneous	Homogeneous	Homogeneous
F III (Extract)	Homogeneous	Homogeneous	Homogeneous
F I (Nano)	Homogeneous	Homogeneous	Homogeneous
F II (Nano)	Homogeneous	Homogeneous	Homogeneous
F III (Nano)	Homogeneous	Homogeneous	Homogeneous

All tested formulations demonstrated complete homogeneity across three replicates, indicating that the active compounds and excipients were uniformly dispersed within the gel matrix. The absence of visible coarse particles or phase separation confirms that the mixing process—conducted at 100 rpm for 30 minutes—was sufficient to achieve a stable and well-integrated system [50].

This result is particularly important for nanoformulations, where particle dispersion can be challenging due to potential agglomeration. The consistent homogeneity observed in both extract-based and nano-based gels suggests that the formulation strategy, including the use of gelatin as a stabilizer, effectively supported uniform distribution of active ingredients [51].

Maintaining homogeneity is essential not only for product stability but also for ensuring reproducible therapeutic or protective effects in topical applications. These findings support the robustness of the preparation method and the compatibility of the selected excipients with both extract and nanoparticle systems.

• pH Evaluation of Sunscreen Gel Formulations

The pH of the sunscreen gel formulations was measured by diluting 1 g of gel with 10 mL of distilled water, followed by immersion of the electrode into the sample. This test was conducted to ensure compatibility with the physiological pH range of human skin.

Table 10. pH test results of sunscreen gel formulations.

Formulation	Mean ± SD
Blank	4.49 ± 0.02
F I (Extract)	4.54 ± 0.02
F II (Extract)	4.71 ± 0.01
F III (Extract)	4.55 ± 0.01
F I (Nano)	4.88 ± 0.03
F II (Nano)	4.84 ± 0.01
F III (Nano)	4.85 ± 0.01

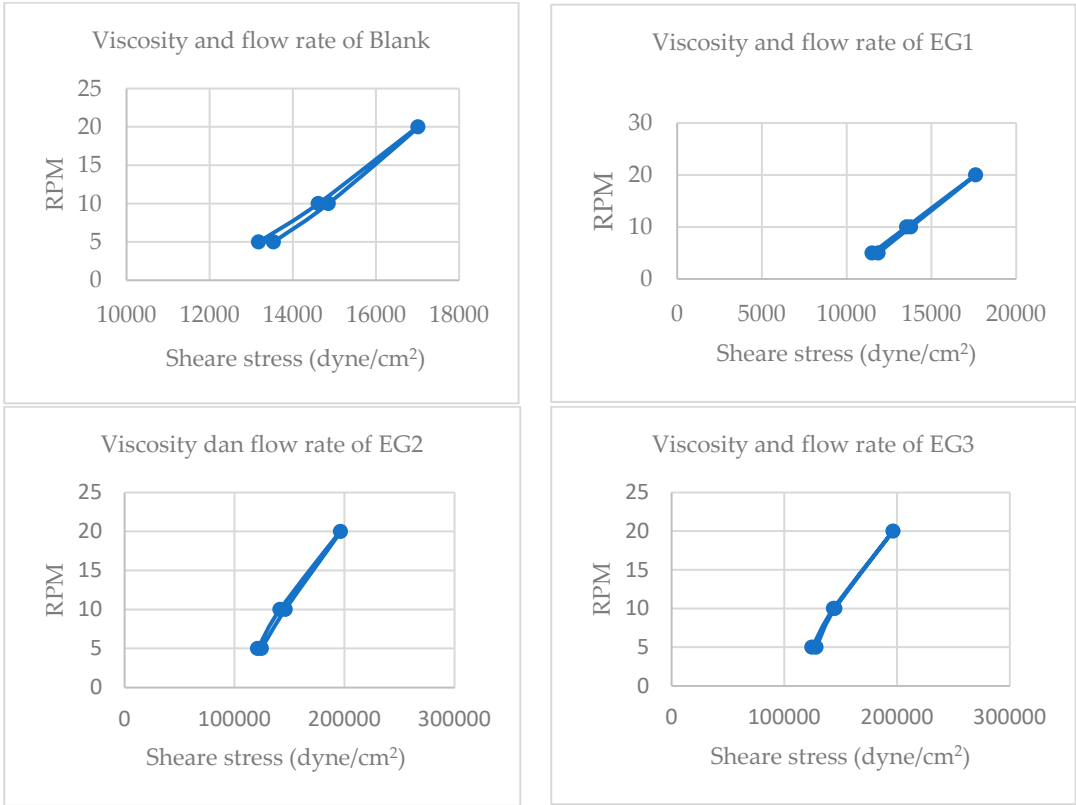
All formulations exhibited pH values within the acceptable skin compatibility range of 4.0–7.5 [52]. The blank formulation showed a mean pH of 4.49 ± 0.02 , while extract-based formulations ranged from 4.54 ± 0.02 to 4.71 ± 0.01 . Nanoformulations demonstrated slightly higher pH values, ranging from 4.84 ± 0.01 to 4.88 ± 0.03 .

The lower pH observed in extract-based gels may be attributed to the presence of acidic phytochemicals. In contrast, the slightly elevated pH in nanoformulations is likely due to the buffering effect of gelatin and other polymers, which can interact with acidic compounds via hydrogen bonding or ionic interactions, thereby reducing overall acidity [51].

Maintaining pH within the physiological range is essential to prevent skin irritation, dryness, and disruption of the stratum corneum barrier. These results confirm that all tested formulations are suitable for topical application and meet dermatological safety standards.

• Viscosity and Flowrate Properties of Gel Formulation

Viscosity testing was conducted to evaluate the rheological behavior of the blank sunscreen gel formulation using a Brookfield viscometer. Measurements were taken across multiple spindle types (5, 6, and 10) and rotational speeds (RPM), generating viscosity values in centipoise (cP) and corresponding shear stress (dyne/cm²).



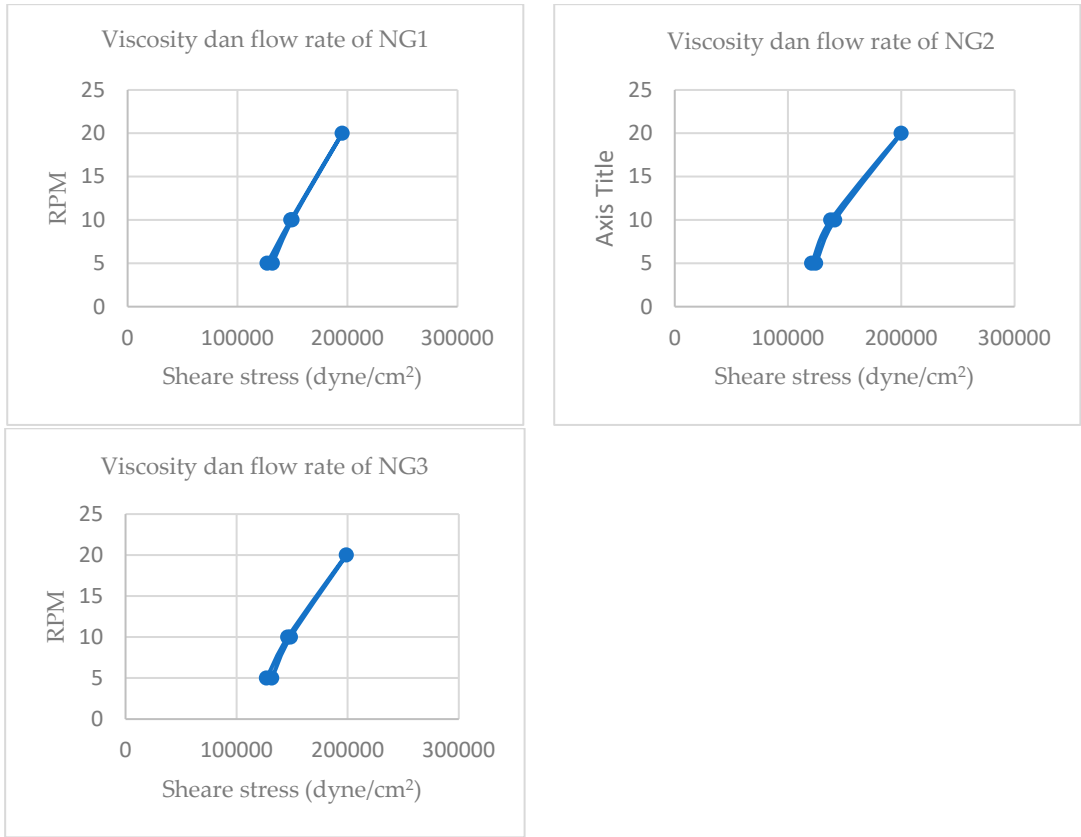


Figure 4. Profiles of viscosities and flow rates of Syzygium gels containing extract (EG) and containing nanoparticles (NG).

The viscosity test aims to determine whether the gel's thickness meets the required standards for topical application. According to SNI 16-4399-1996, the acceptable viscosity range for gel preparations is 6000–50000 cP [53]. All tested formulations—both extract-based and nanoparticle-based—fall within this range, indicating compliance with national standards and suitability for topical use.

Viscosity results:

- *Extract-Based Formulations*, F I (12,330 cP), F II (13,667 cP), and F III (13,667 cP), with a relationship $F I < F II = F III$.
- *Nanoparticle-Based Formulations*, F I (13,583 cP), F II (13,917 cP), F III (13,833 cP), with a relationship $F I < F II > F III$

The viscosity values of all formulations fall within the optimal range for gel-based sunscreens, ensuring adequate spreadability and user comfort. Notably, nanoparticle-based formulations exhibit slightly higher viscosity than their extract-based counterparts, which may be attributed to the increased surface area and interaction of nanoparticles with the gel matrix. F II consistently shows the highest viscosity in both groups, suggesting a potential influence of active concentration or stabilizer content. [54]

Flow curve analysis reveals plastic flow behavior across all formulations, characterized by a yield stress threshold before flow initiation [55]. This rheological profile is advantageous for topical gels, as it prevents premature spreading and particle sedimentation, thereby enhancing product stability and uniformity during storage and application.

These findings support the formulation's physical integrity and suggest that nanoparticle incorporation does not compromise viscosity but may enhance structural consistency. Further investigation into the correlation between viscosity and active release kinetics is recommended to optimize therapeutic performance.

- Spreadability

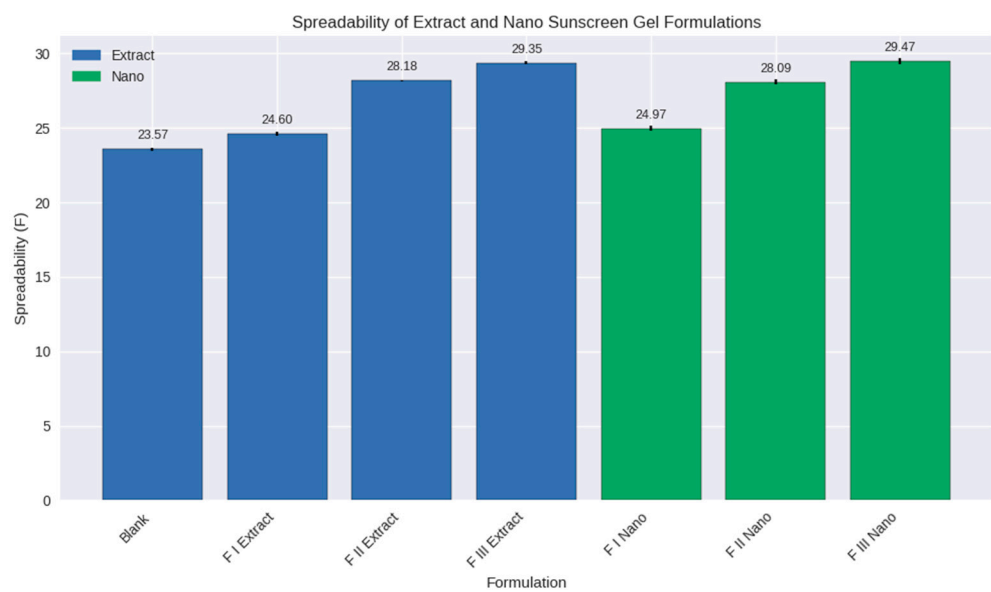


Figure 5. Spreadability of formulations of Blank, containing extract (FI, FII, and FIII), and containing nanoparticles (FI, FII, and FIII).

The spreadability test confirmed that all sunscreen gel formulations fell within the acceptable range of 5–7 cm, ensuring ease of application and uniform coverage on the skin. However, notable differences were observed betwthe blank, extract-based, and nanoformulations. The blank gel exhibited the lowest spreadability (23.57 ± 0.09), reflecting the baseline rheological properties of the gel matrix without active compounds. Extract-based formulations showed progressive increases in spreadability, with F III Extract reaching 29.35 ± 0.10 , suggesting that higher extract concentrations contributed to reduced internal resistance and improved gel fluidity.

Nanoformulations demonstrated the highest spreadability values, with F III Nano achieving 29.47 ± 0.20 . This superior performance can be attributed to the nanoparticle dispersion and stabilizing effect of gelatin, which enhance the uniform distribution of active compounds and reduce particle aggregation. The improved spreadability of nanoformulations complements their previously observed rheological and pH characteristics: slightly higher pH values due to buffering interactions and pseudoplastic flow behavior that facilitates spreading under shear. Together, these properties highlight the multifunctional role of gelatin as both a stabilizer and a rheology modifier [56,57].

From a practical perspective, enhanced spreadability is critical for sunscreen formulations, as it ensures uniform film formation, maximizes UV protection, and improves consumer acceptability. Poorly spreadable gels may leave uneven coverage, leading to reduced efficacy and potential skin irritation. The results therefore suggest that nanoformulations not only improve the physicochemical stability of the gel but also enhance its functional performance during topical application. In conclusion, the comparative analysis demonstrates that while all formulations are dermatologically acceptable, nanoformulations provide the most favorable balance of spreadability, viscosity, and pH compatibility, positioning them as promising candidates for advanced sunscreen delivery systems.

- Stability
 - Organoleptic evaluation before and after cyclng

Organoleptic assessment was conducted both before and after the cycling test.

Table 11. Organoleptic evaluation of sunscreen gel (before cycling).

Before cycling									
Formulation	Form			Color			Odor		
Blank	Thick	Thick	Thick	Colorless	Colorless	Colorless	Charac.	Charac.	Charac.
F I (extract)	Thick	Thick	Thick	L yellow	L yellow	L yellow	Charac.	Charac.	Charac.

F II (extract)	Thick	Thick	Thick	P yellow	P yellow	P yellow	Charac.	Charac.	Charac.
F III (extract)	Thick	Thick	Thick	Yellow	Yellow	Yellow	Charac.	Charac.	Charac.
F I (nanoparticles)	Thick	Thick	Thick	P yellow	P yellow	P yellow	Charac.	Charac.	Charac.
F II (nanoparticles)	Thick	Thick	Thick	Turbid	Turbid	Turbid	Charac.	Charac.	Charac.
F III (nanoparticles)	Thick	Thick	Thick	Turbid	Turbid	Turbid	Charac.	Charac.	Charac.
L yellow: Light yellow; P yellow: Pale yellow; Charac.: Characteristic									

Table 12. Organoleptic evaluation of sunscreen gel (after cycling).

Before cycling									
Formulation	Form			Color			Odor		
Blank	Thick	Thick	Thick	Colorless	Colorless	Colorless	Charac.	Charac.	Charac.
F I (extract)	Thick	Thick	Thick	L yellow	L yellow	L yellow	Charac.	Charac.	Charac.
F II (extract)	Thick	Thick	Thick	P yellow	P yellow	P yellow	Charac.	Charac.	Charac.
F III (extract)	Thick	Thick	Thick	Yellow	Yellow	Yellow	Charac.	Charac.	Charac.
F I (nanoparticles)	Thick	Thick	Thick	P yellow	P yellow	P yellow	Charac.	Charac.	Charac.
F II (nanoparticles)	Thick	Thick	Thick	Turbid	Turbid	Turbid	Charac.	Charac.	Charac.
F III (nanoparticles)	Thick	Thick	Thick	Turbid	Turbid	Turbid	Charac.	Charac.	Charac.
L yellow: Light yellow; P yellow: Pale yellow; Charac.: Characteristic									

The organoleptic examination following the cycling stability test was conducted to determine whether the sunscreen gel formulation underwent any changes in physical characteristics—specifically texture, color, and odor. These parameters were observed before and after exposure to alternating temperature conditions. Any alteration in these attributes may indicate formulation instability, potentially compromising product efficacy and safety.

Based on the results, no changes were observed in texture, color, or odor across all formulations before and after the cycling test. This consistency indicates that the sunscreen gel maintains organoleptic stability even after exposure to extreme temperature variations. Such stability suggests that the formulation possesses robust physical integrity and is capable of preserving its sensory characteristics under stress conditions.

The absence of organoleptic changes post-cycling test reflects the formulation’s resilience against thermal stress, which is critical for maintaining consumer acceptance and product performance during storage and distribution. Stability in texture and color implies that the emulsion system remains intact, while consistent odor suggests no degradation of active or aromatic compounds. These findings align with previous studies emphasizing the importance of excipient selection and gel matrix design in achieving thermally stable topical formulations. [49,56]

- Homogeneity evaluation before and after cycling

Table 12. Homogeneity evaluation of sunscreen gel (before cycling).

Before cycling			
Formulation	1	2	3
Blank	Homogeneous	Homogeneous	Homogeneous
F I (extract)	Homogeneous	Homogeneous	Homogeneous
F II (extract)	Homogeneous	Homogeneous	Homogeneous
F III (extract)	Homogeneous	Homogeneous	Homogeneous
F I (nanoparticles)	Homogeneous	Homogeneous	Homogeneous
F II (nanoparticles)	Homogeneous	Homogeneous	Homogeneous
F III (nanoparticles)	Homogeneous	Homogeneous	Homogeneous

Table 13. Homogeneity evaluation of sunscreen gel (after cycling).

Formulation	After cycling		
	1	2	3
Blank	Homogeneous	Homogeneous	Homogeneous
F I (extract)	Homogeneous	Homogeneous	Homogeneous
F II (extract)	Homogeneous	Homogeneous	Homogeneous
F III (extract)	Homogeneous	Homogeneous	Homogeneous
F I (nanoparticles)	Homogeneous	Homogeneous	Homogeneous
F II (nanoparticles)	Homogeneous	Homogeneous	Homogeneous
F III (nanoparticles)	Homogeneous	Homogeneous	Homogeneous

Homogeneity testing is essential to ensure that active compounds and excipients are evenly distributed throughout the gel matrix, thereby guaranteeing consistent therapeutic performance and consumer acceptability. As shown in Tables 12 and 13, all formulations—blank, extract-based, and nanoparticle-based—remained homogeneous before and after the cycling stability test. No phase separation, sedimentation, or visual inconsistencies were observed, confirming that the gels maintained structural integrity under thermal stress.

The consistent homogeneity observed in nanoparticle formulations highlights the stabilizing role of polymers such as Carbopol and HPMC, which form a robust gel network capable of suspending dispersed particles uniformly. This finding is particularly relevant for nanoparticle systems, where aggregation risk is higher due to increased surface energy. The ability of the gel matrix to maintain uniformity under stress conditions supports the physical stability of the formulations and validates their suitability for long-term topical application.

Previous studies have emphasized that homogeneity is a critical parameter in sunscreen and topical gel formulations, directly linked to product stability and consumer perception. For instance, formulations containing natural extracts demonstrated stable homogeneity and physical properties even after stress testing [58]. Similarly, nanoparticle-loaded gels have been shown to maintain uniform distribution of active compounds, enhancing both stability and bioavailability [59]. These findings corroborate the present results, where both extract-based and nanoparticle-based gels exhibited excellent homogeneity before and after cycling.

- pH evaluation before and after cycling

Table 14. pH test results of sunscreen gel formulations (before and after cycling).

Formula	pH Before Cycling (Mean ± SD)	pH After Cycling (Mean ± SD)
Blank	4.49 ± 0.02	5.64 ± 0.01
F I (Extract)	4.54 ± 0.02	5.67 ± 0.02
F II (Extract)	4.71 ± 0.01	5.64 ± 0.02
F III (Extract)	4.55 ± 0.01	5.37 ± 0.02
F I (Nano)	4.89 ± 0.03	5.17 ± 0.02
F II (Nano)	4.83 ± 0.03	5.34 ± 0.01
F III (Nano)	4.85 ± 0.01	5.64 ± 0.01

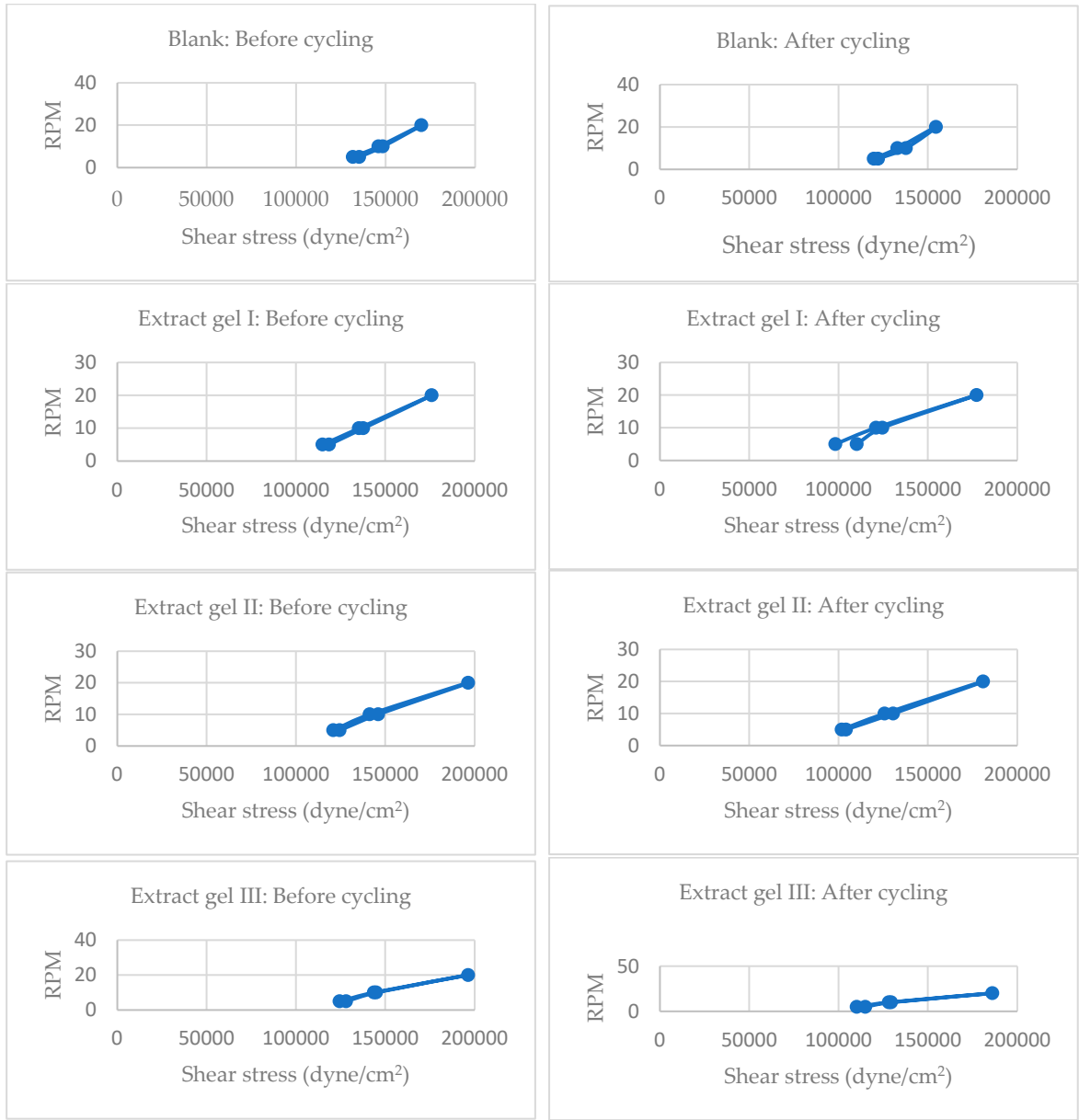
The pH stability of sunscreen gel formulations is a critical parameter influencing both product safety and efficacy. In this study, all formulations exhibited an increase in pH following the cycling test, which simulates temperature fluctuations and mechanical stress during storage. The blank formulation showed the most pronounced pH shift (from 4.49 ± 0.02 to 5.64 ± 0.01), suggesting limited buffering capacity or absence of stabilizing agents.

Formulations containing extract (F I–F III) also demonstrated pH elevation, with F II (Extract) maintaining the highest pre-cycling pH (4.71 ± 0.01) and a moderate post-cycling value (5.64 ± 0.02). This may reflect the influence of phytochemical constituents, such as polyphenols and flavonoids, which can interact with excipients and affect pH resilience.

Interestingly, nano-formulated variants (F I-F III Nano) showed smaller pH shifts, particularly F I (Nano), which changed from 4.89 ± 0.03 to 5.17 ± 0.02 . This suggests that nanoencapsulation may enhance pH stability by protecting active compounds from environmental stressors and reducing their direct interaction with the gel matrix. Such findings align with previous reports indicating that nanoscale delivery systems can improve the physical stability of sunscreen gels, including pH, viscosity, and spreadability.

Overall, the results support the hypothesis that nanoformulation contributes to better pH retention under stress conditions, which is essential for maintaining product performance and minimizing skin irritation risk. These insights are valuable for optimizing sunscreen gel formulations intended for tropical climates with variable storage conditions [60–62].

- Viscosity before and after cycling



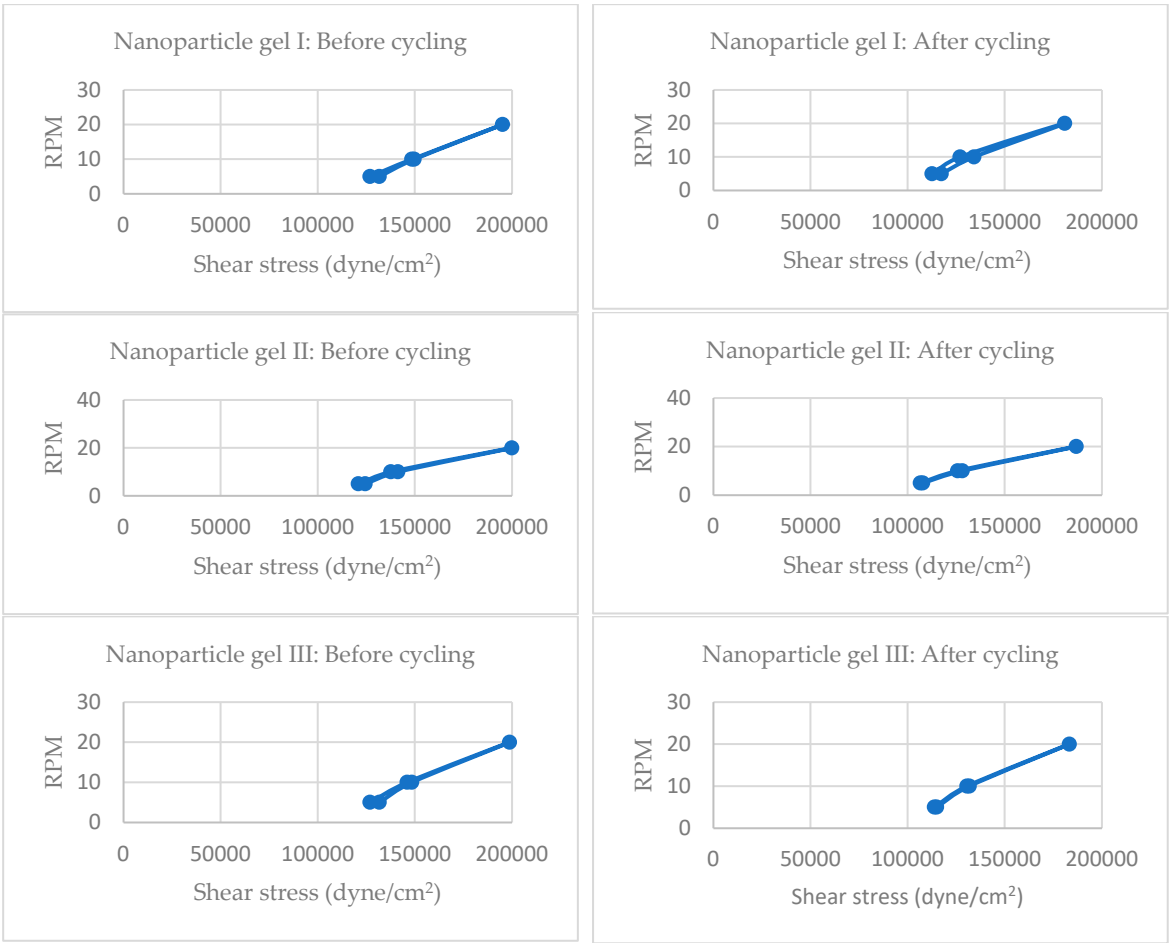


Figure 6. Cycling test data on viscosity before and after cycling of Blank, Extract and Nanoparticle Formulations.

Overview of Cycling Impact

Cycling refers to repeated stress or temperature exposure, simulating long-term storage or usage. Stability is inferred from changes in shear stress at fixed RPMs—smaller changes suggest better structural resilience.

Extract Gel Formulations

Before Cycling:

- Shear stress values at 5 RPM range from ~114,992 to 128,168 dyne/cm².
- At 20 RPM, values reach up to ~196,445 dyne/cm², indicating strong resistance to flow under high shear.

After Cycling:

- Shear stress at 5 RPM drops to ~98,222–114,992 dyne/cm².
- At 20 RPM, values decrease to ~124,575–186,862 dyne/cm².

Interpretation:

- Significant reduction in shear stress post-cycling, especially at low RPMs, suggests partial breakdown of gel matrix or reduced internal cohesion.
- The drop is more pronounced in extract gels, indicating lower rheological stability under stress.

Nano Gel I Formulations

Before Cycling:

- Shear stress at 5 RPM ranges from ~120,981 to 131,762 dyne/cm².
- At 20 RPM, values reach ~195,247–200,004 dyne/cm².

- After Cycling:
- Shear stress at 5 RPM drops to ~106,607–117,388 dyne/cm².
 - At 20 RPM, values remain relatively high: ~180,873–186,862 dyne/cm².
- Interpretation:
- Moderate reduction in shear stress after cycling, but values remain higher than extract gels.
 - Indicates better structural retention, likely due to gelatin nanoparticle reinforcement and encapsulation effects.
 - Nano gels show enhanced resilience to mechanical stress, supporting their use in long-term topical applications.

Comparative Stability Summary

Formulation	Shear stress drop (5 RPM)	Shear stress drop (20 RPM)	Stability After Cycling
Extract Gel	~10–20%	~10–30%	Moderate to Low
Nano Gel I	~5–15%	~5–10%	High

Conclusion

Nano gel formulations exhibit superior rheological stability compared to extract gels after cycling. This supports your hypothesis that nanoparticle incorporation enhances gel integrity, likely due to better polymeric network formation and reduced degradation under stress. [63,64]

- Spreadability

Table 15. Spreadability test results of gel formulations (before and after cycling).

Formula	Diameter (cm)	Spreadability (F)
Blank	5.48 ± 0.01	23.57 ± 0.09
F I (Extract)	5.61 ± 0.01	24.68 ± 0.11
F II (Extract)	5.99 ± 0.01	28.12 ± 0.12
F III (Extract)	6.12 ± 0.01	29.35 ± 0.10
F I (Nano)	5.64 ± 0.02	24.97 ± 0.18
F II (Nano)	5.98 ± 0.02	28.09 ± 0.16
F III (Nano)	6.13 ± 0.02	29.47 ± 0.20

Spreadability reflects the ease of topical application and uniform distribution of gel on the skin. It is influenced by viscosity, polymer concentration, and structural integrity.

- Blank gel shows the lowest spreadability (23.57 ± 0.09), serving as a baseline.
- Extract gels (Formulas I–III) show increasing spreadability with higher extract concentration, peaking at Formula III (29.35 ± 0.10).
- Nano gels (Formulas I–III) exhibit similar or slightly higher spreadability than their extract counterparts, with Formula III Nano reaching the highest value (29.47 ± 0.20).

Interpretation:

- Cycling did not significantly reduce spreadability, indicating good physical stability.
- Nano formulations maintain or slightly improve spreadability, likely due to better dispersion and reduced particle aggregation.
- These results align with rheological data showing nano gels retain shear stress better after cycling, confirming their superior structural resilience.

Based on the SPSS output using two-way ANOVA statistical analysis, the significance value (Sig.) for the normality test was 0.401 and for the homogeneity test was 0.945, both exceeding 0.05 and thus meeting the assumptions for parametric testing. The ANOVA test yielded a Sig. value of 0.931 (> 0.05), indicating that there is no significant interaction between the formula used and the storage conditions in determining the viscosity of the preparation. Therefore, the null hypothesis (H₀) is accepted, and the alternative hypothesis (H₁) is rejected. [65,66]

- Formulation SPF before and after cycling

SPF Determination of Sunscreen Gel Formulations:

The Sun Protection Factor (SPF) values of the sunscreen gel formulations were calculated using spectrophotometric absorbance data across UV wavelengths ranging from 290 to 320 nm. The SPF was determined using the Mansur equation: [67]

$$SPF = CF \times \sum (EE \times I \times Abs)$$

CF is the correction factor (typically 10), $EE \times I$ represents the erythema effect and solar intensity at each wavelength, and Abs is the absorbance of the sample.

The grouped bar chart showed SPF values of extract and nano gels before and after cycling. It highlights how nano formulations consistently maintain slightly higher SPF values and better stability compared to extract gels:

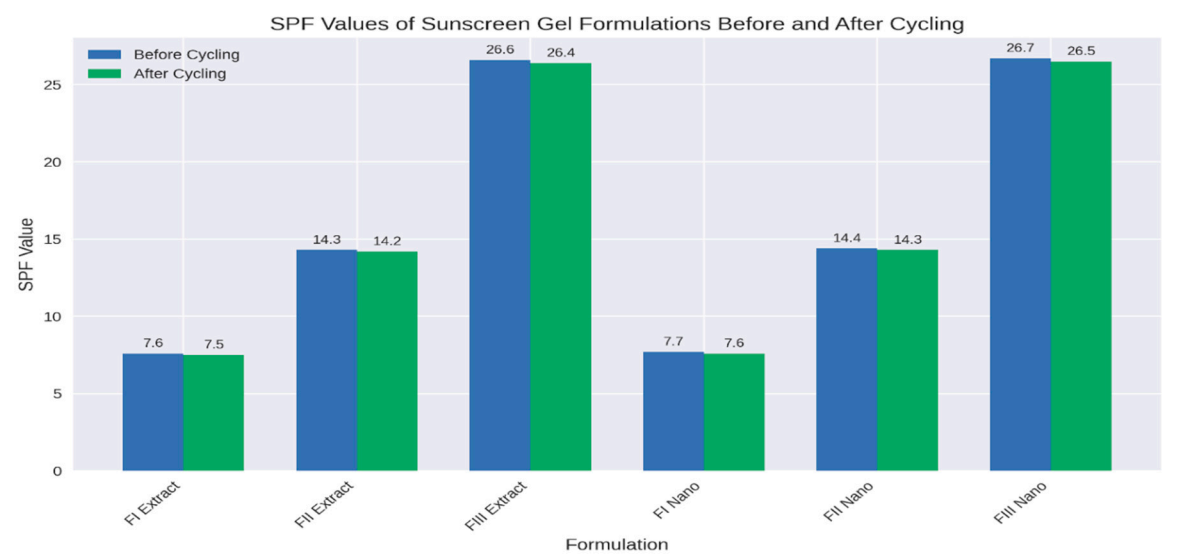


Figure 7. Nano gels outperform extract gels in SPF retention, especially at higher concentrations (Formula III).

Figure 7 shows clearly that while both systems are stable under cycling, nano gels outperform extract gels in SPF retention, especially at higher concentrations (Formula III). The bar chart compared SPF values of extract and nano gels before and after cycling. It clearly shows the stability advantage of the nano formulations:

Extract gels: FI (7.6 → 7.5), FII (14.3 → 14.2), FIII (26.6 → 26.4)

Nano gels: FI (7.7 → 7.6), FII (14.4 → 14.3), FIII (26.7 → 26.5)

Moreover, SPF values can be expressed as percentage of UV blocking to make them more intuitive. The general approximation is:

$$\% \text{ UV Blocking} = (1 - (1/SPF)) \times 100$$

Low SPF (FI) blocks ~87% of UV radiation, suitable only for short exposure. Medium SPF (FII) blocks ~93%, offering moderate protection. High SPF (FIII) blocks ~96%, providing strong protection. Nano gels consistently show slightly higher % blocking compared to extract gels, confirming their enhanced photoprotective performance and stability after cycling. [68–70]

Table 16. Calculated % UV blocking.

Formula	SPF (Before)	% Blocking (Before)	SPF (After)	% Blocking (After)
FI Extract	7.6	86.8%	7.5	86.7%
FII Extract	14.3	93.0%	14.2	92.9%
FIII Extract	26.6	96.2%	26.4	96.2%
FI Nano	7.7	87.0%	7.6	86.8%
FII Nano	14.4	93.1%	14.3	93.0%
FIII Nano	26.7	96.3%	26.5	96.2%

- Antioxidant activity of formulations before and after cycling

Table 17. Antioxidant activity of formulations before and after cycling.

Formulations	Before cycling	After cycling
FI Extract	52.78 ± 0.13	52.76 ± 0.59
FII Extract	49.30 ± 0.05	48.14 ± 0.38
FIII Extract	41.09 ± 0.13	40.85 ± 0.34
FI Nano	80.27 ± 0.56	80.24 ± 0.52
F II Nano	72.99 ± 0.08	72.92 ± 0.08
F III Nano	67.39 ± 0.03	67.74 ± 0.63

Antioxidant Stability Before and After Cycling

All formulations maintained strong antioxidant activity following thermal cycling, with minimal changes in IC₅₀ values, indicating robust stability of bioactive compounds under stress conditions.

- **Extract-based gels** showed slight reductions in antioxidant potency post-cycling, particularly FII (↓1.16 ppm) and FIII (↓0.24 ppm), suggesting moderate sensitivity of polyphenolic constituents to thermal fluctuations. However, the changes remained within acceptable limits, with IC₅₀ values still below 100 ppm, confirming pharmacological relevance.
- **Nano-based gels** demonstrated superior stability, with FI and FII showing negligible shifts (<0.1 ppm), and FIII even exhibiting a slight improvement (↑0.35 ppm), possibly due to enhanced dispersion or release kinetics post-cycling. The consistently low standard deviations (e.g., FII Nano: ±0.08) further underscore the reproducibility and robustness of the nanoparticle system.

These results affirm that **nanoparticle encapsulation enhances thermal resilience**, preserving antioxidant efficacy during formulation stress. The findings support the suitability of nano-delivery systems for cosmeceutical applications requiring long-term stability. [71]

- Franz Diffusion Profiles of Flavonoid Penetration

The Franz diffusion test was conducted to evaluate the transdermal penetration of flavonoids from extract and nanoparticle formulations of *Syzygium myrtifolium* over time. The cumulative amount of flavonoid penetrated (Q) was measured at intervals up to 200 minutes using UV-VIS spectrophotometry. [72]

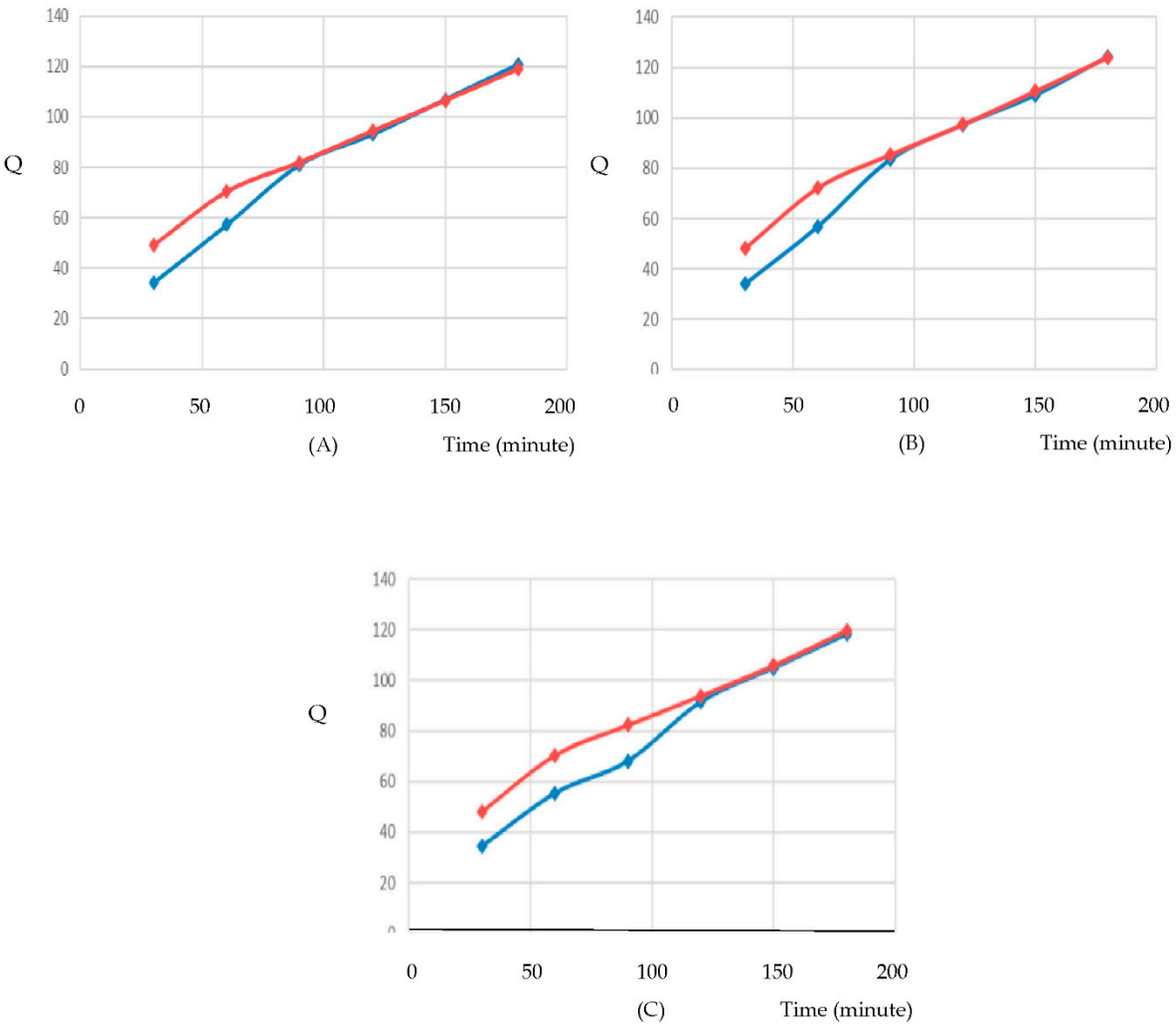


Figure 8. Relationship between time and Q for F I, F II, and F III.

Comparative Analysis:

- **F I:**
Nanoparticle FI showed significantly higher penetration than Extract FI, with Q values reaching approximately 120 units at 180 minutes, compared to ~90 units for the extract. This suggests enhanced delivery due to nanoparticle encapsulation. [72]
- **F II:**
Similar trends were observed. Nanoparticle FII reached ~120 units, while Extract FII plateaued around ~100 units. The difference in slope indicates faster and more efficient diffusion from the nanoparticle system. [72]
- **F III:**
Nanoparticle FIII again outperformed Extract FIII, with Q values nearing 120 units versus ~100 units for the extract. The consistency across all formulas confirms the superior permeation profile of the nanoparticle formulations. [72,73]

Across all three formulas, nanoparticle systems consistently demonstrated:

- Higher cumulative penetration (Q)
- Steeper diffusion curves
- Faster onset of permeation

These results validate the use of gelatin-based nanoparticles for enhancing skin delivery of flavonoid-rich botanical extracts, supporting their application in cosmeceutical formulations targeting antioxidant and photoprotective effects. [72,73]

Permeation Parameters of Flavonoid Formulations via Franz Diffusion Cell

The table below summarizes the results of Franz diffusion testing for three formulations (F I, F II, F III) in both extract and nanoparticle forms. Key parameters include flux ($\mu\text{g}/\text{cm}^2/\text{h}$), permeability constant (cm/h), and diffusion coefficient (cm^2/h).

Table 18. Summary of Franz diffusion penetration test.

Parameter	Flux ($\mu\text{g}/\text{cm}^2/\text{h}$)	Permeability Constant (cm/h)	Diffusion Coefficient (cm^2/h)
F1 (Nanoparticle)	0.5633	0.1616	0.1092
F2 (Nanoparticle)	0.5904	0.0954	0.1145
F3 (Nanoparticle)	0.5633	0.0910	0.1092
F1 (Extract)	0.4451	0.0719	0.0863
F2 (Extract)	0.4827	0.0780	0.0936
F3 (Extract)	0.4527	0.0731	0.0878

- Packaging



Figure 9. Example of *Syzygium myrtifolium* sunscreen gels in HDPE tubes.

3. Conclusions

Syzygium myrtifolium (red shoot leaves) contains flavonoids with strong antioxidant and photoprotective properties, supporting its potential as a natural sunscreen agent. Gel formulations prepared from both crude extract and nanoparticle forms demonstrated acceptable physicochemical and organoleptic characteristics. Antioxidant testing (DPPH assay) revealed very strong activity, with IC50 values of 32.59 ± 0.18 ppm, while SPF evaluation confirmed concentration-dependent UV protection. Franz diffusion studies showed that nanoparticle formulations enhanced skin permeation, flux, and diffusion coefficients compared to extract gels. However, extract-based gels exhibited higher SPF and antioxidant activity, indicating stronger direct photoprotective potential. Overall, these findings highlight *S. myrtifolium* gels as promising natural cosmeceutical formulations. Extract gels are particularly effective as antioxidant-rich sunscreens, while nanoparticle systems offer advantages in controlled release and skin penetration. Together, they provide a safer and more sustainable approach to skin photoprotection and support the broader application of Indonesian medicinal plants in cosmeceutical innovation. Here are the highlights of your article, formatted in MDPI style (concise bullet points emphasizing novelty and contribution):

Highlights:

- *Syzygium myrtifolium* (red shoot leaves) is identified as a rich source of flavonoids with strong antioxidant and photoprotective properties.
- Gel formulations were successfully prepared using both crude extract and nanoparticle forms, with acceptable physicochemical and organoleptic characteristics.
- The extract-based gel demonstrated higher SPF values and antioxidant activity compared to the nanoparticle gel, confirming its strong photoprotective potential.
- Franz diffusion studies revealed that nanoparticle gels exhibited enhanced skin permeation, flux, and diffusion coefficients**, supporting controlled release and deeper delivery.
- Findings highlight the dual potential: extract gels as effective natural sunscreens, and nanoparticle gels as advanced delivery systems, contributing to safer and more sustainable approaches to skin photoprotection.

Novelty Statement:

This study is the first to comprehensively evaluate *Syzygium myrtifolium* (red shoot leaves) gel formulations for photoprotective applications, comparing crude extract and nanoparticle forms. While nanoparticles enhanced skin permeation, flux, and diffusion coefficients, the extract-based gels demonstrated superior SPF and antioxidant activity. The dual findings highlight a unique balance between immediate photoprotection (extract gels) and controlled release with deeper penetration (nanoparticle gels).

This integrated approach underscores the potential of *S. myrtifolium* as a sustainable, plant-derived cosmeceutical, advancing the use of Indonesian medicinal plants in global sunscreen innovation.

4. Materials and Methods

4.1. Materials

- Primary material: Fresh red leaves of *Syzygium myrtifolium* Walp. (commonly known as pucuk merah) were collected from the garden of Faculty of Pharmacy, Universitas Pancasila, Jakarta, Indonesia.
- Additional materials: Ethanol 70% (Merck, Darmstadt, Germany), hydrochloric acid 1% (Merck, Darmstadt, Germany), 2,2-diphenyl-1-picrylhydrazyl (DPPH; Sigma-Aldrich, St. Louis, MO, USA), Vitamin C reference standard (Sigma-Aldrich, St. Louis, MO, USA), ethanol 96% (Merck, Darmstadt, Germany), methanol PA (Merck, Darmstadt, Germany), dimethyl sulfoxide (DMSO; Sigma-Aldrich, St. Louis, MO, USA), gelatin (Sigma-Aldrich, St. Louis, MO, USA), poloxamer 188 (Sigma-Aldrich, St. Louis, MO, USA), glutaraldehyde 2% (Merck, Darmstadt, Germany), carbomer 940 (Sigma-Aldrich, St. Louis, MO, USA), propylene glycol (Merck, Darmstadt, Germany), phenoxyethanol (Sigma-Aldrich, St. Louis, MO, USA), triethanolamine (Merck, Darmstadt, Germany), and purified water (local pharmaceutical grade, Jakarta, Indonesia).

4.2. Equipment

The instruments used in this study included: analytical balance (Kern, Balingen, Germany), oven (Mettler U-30, Mettler GmbH, Schwabach, Germany), rotary vacuum evaporator (Heidolph, Schwabach, Germany), magnetic stirrer (IKA Eurostar, IKA Werke GmbH, Staufen, Germany), viscometer (Brookfield RV type, Brookfield Engineering Laboratories, Middleboro, MA, USA), water bath (Mettler W 600, Mettler GmbH, Schwabach, Germany), pH meter (Hanna Instruments, Woonsocket, RI, USA), Karl Fischer titrator (Metrohm AG, Herisau, Switzerland), UV-Vis spectrophotometer (Shimadzu, Kyoto, Japan), standard laboratory glassware (Pyrex, Corning Inc., NY, USA; Iwaki, Asahi Glass Co., Tokyo, Japan), microscope (Optika, Ponteranica, Italy), micropipettes (Eppendorf, Hamburg, Germany), thermometer (IKA Werke GmbH, Staufen, Germany), glass slides (Matsunami Glass Ind., Osaka, Japan), evaporating dishes (Corning Inc., NY, USA), stirring rods (Pyrex, Corning Inc., NY, USA), spatulas (Fisher Scientific, Waltham, MA, USA), filter paper (Whatman, Maidstone, UK), aluminum foil (Reynolds, Richmond, VA, USA), blender

(Philips, Amsterdam, Netherlands), sieves no. 4 and no. 18 (Retsch GmbH, Haan, Germany), cuvettes (Hellma Analytics, Müllheim, Germany), refrigerator (Panasonic, Osaka, Japan), dropper pipettes (Fisher Scientific, Waltham, MA, USA), mortar and pestle (Corning Inc., NY, USA), parchment paper (Fisher Scientific, Waltham, MA, USA), hot plate (IKA Werke GmbH, Staufen, Germany), and plastic tube containers (Falcon, Corning Inc., NY, USA).

4.3. Methods

4.3.1. Materials and Botanical Identification

a. Plant Material Preparation

Fresh red shoot leaves (*Syzygium myrtifolium* Walp.) were collected from the campus area of Universitas Pancasila, Jakarta, Indonesia. The leaves were subjected to wet sorting to remove foreign matter and debris, washed under running water, sliced, and dried in an oven at 40 °C. The dried leaves were then powdered using a blender and sieved through mesh no. 4 and no. 18. The resulting powder was stored in clean, dry, tightly sealed containers protected from light. [74,75]

b. Botanical Determination

The botanical identification of *Syzygium myrtifolium* Walp. was carried out at the Herbarium Depokensis (UIDEP), Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, Indonesia. The plant specimen was authenticated by a taxonomist, and a voucher specimen was deposited for reference. [74,75]

c. Fineness Degree of *Syzygium myrtifolium* Simplicia

The powdered simplicia was evaluated for fineness degree according to pharmacognostic standards. The powder was passed through sieves no. 4 and no. 18, and the proportion retained was recorded. The fineness degree was expressed as the percentage of powder passing through the designated mesh size, following standard pharmacopoeial procedures. [74,75]

4.3.2. Preparation of *Syzygium myrtifolium* Extract

a. Extract Preparation

The ethanol extract of red shoot leaves was prepared using the maceration method with 70% ethanol as a polar solvent. One kilogram of simplicia powder was macerated in 1 liter of 70% ethanol for 2 × 24 hours. The macerate was filtered and concentrated using a rotary vacuum evaporator at 40 °C to obtain a thick extract. The extract was weighed, and the yield and drug-extract ratio (DER) were calculated using the following formula [16]:

$$\text{Yield (\%)} = (\text{Weight of Extract} / \text{Weight of Simplicia}) \times 100\%$$

$$\text{Extraction yield and DER-native value} = \text{Weight of Simplicia} / \text{Weight of Extract}$$

b. Phytochemical Screening of Extract

The concentrated ethanol extract of *Syzygium myrtifolium* Walp. was subjected to qualitative phytochemical screening using standard pharmacognostic procedures [27].

- Alkaloids: Detected using Mayer's and Dragendorff's reagents; positive indicated by yellow or orange coloration.
- Flavonoids: Identified by reaction with magnesium powder, amyl alcohol, and concentrated HCl; red, yellow, or orange coloration indicated presence.
- Saponins: Confirmed by stable foam formation after heating with water and HCl 2 N.

c. Specific and Non-specific Parameters of *Syzygium myrtifolium* Extract

Specific Parameters of *Syzygium myrtifolium* Extract [76]:

The extract was assessed for organoleptic properties, pH, and solubility profile:

- Organoleptic evaluation: The extract exhibited a thick consistency, a characteristic tea-like odor, and a deep red color, consistent with polyphenol-rich materials such as anthocyanins and

flavonoids. Organoleptic testing was performed by observing physical form, aroma, and color [12,26].

- pH measurement: Using a calibrated electrode, the diluted extract showed a certain pH, indicating acidity favorable for antioxidant stability in topical formulations [27].
- Solubility testing: Conducted in various solvents according to pharmacopoeial standards. The extract was soluble or insoluble in distilled water, propylene glycol, ethanol 96%, and DMSO. These results suggest compatibility with polar organic solvents, supporting applications in hydrogel, emulgel, and nanoemulsion systems [28,29].

Non-Specific Parameters of *Syzygium myrtifolium* Extract [76]:

General quality attributes were determined following pharmacognostic and pharmacopoeial guidelines:

- Ash content: Total ash averaged below 14%, while acid-insoluble ash was 2.0%, indicating minimal contamination from silicates or soil particles [30].
- Moisture content: Measured at below the 10% threshold recommended for microbial safety and extract stability [30].
- Heavy metal analysis: Atomic Absorption Spectrophotometry (AAS) revealed Pb < 0.05 µg/mL and Cd < 0.02 µg/mL, meeting pharmacopoeial safety limits and confirming suitability for cosmeceutical applications [31].

d. SPF values of *Syzygium myrtifolium* extract

In vitro SPF was determined spectrophotometrically using the Mansur method, which estimates SPF from UV absorbance between 290–320 nm weighted by erythral effect and correction factors. This approach is widely applied to plant extracts and essential oils for preliminary screening.

Sample preparation:

- Extract solution: Dissolve a known mass of the dried extract in ethanol 96% (or another validated solvent with minimal UV background) to a target concentration (e.g., 0.1–1.0 mg/mL), selected to keep absorbance within the linear range (typically $A < 2$).
- Blank: Use the solvent alone in a matched cuvette for baseline correction.
- Cuvettes: Quartz cuvettes with 1 cm path length, cleaned and inspected for scratches.

UV–Vis measurement:

- Wavelength range: Record absorbance from 290 to 320 nm at 5 nm intervals (i.e., 290, 295, 300, 305, 310, 315, 320 nm).
- Baseline: Zero the instrument with the solvent blank.
- Replicates: Measure at least three independent preparations; average the absorbance at each wavelength.
- Instrument settings: Ensure slit width and scan speed provide stable readings; verify lamp performance and cuvette alignment.

SPF Calculation (Mansur Method) [67]:

- Equation:

$$SPF = CF \times \sum (EE(\lambda) \times I(\lambda) \times Abs(\lambda))$$

SPF: Sun Protection Factor, the final measure of the sample's ability to protect against ultraviolet B (UVB) radiation, which is the primary cause of sunburn; CF: Correction Factor, a constant value typically set to 10; $\sum$ sum of: Summation symbol, indicating that the values are summed up across the relevant wavelength range; $EE(\lambda)$: Erythral Effect Spectrum at a specific wavelength (λ). This refers to the potential of UV radiation at that wavelength to cause skin redness or sunburn; $I(\lambda)$: Solar Intensity Spectrum at a specific wavelength (λ). This represents the intensity of the sun's radiation at that wavelength; $Abs(\lambda)$: Absorbance of the sample at a specific wavelength (λ). This value is measured using a UV-Vis spectrophotometer.

Moreover, SPF values can be expressed as percentage of UV blocking to make them more intuitive. The general approximation is:

$$\% \text{ UV Blocking} = (1 - (1/\text{SPF})) \times 100.$$

Interpretation and limitations: Screening purpose: In vitro SPF provides comparative screening for extracts and formulations; it does not replace in vivo determination (ISO 24444) or broad-spectrum testing (UVA-PF, critical wavelength). Formulation effects: SPF of the raw extract may differ in finished dosage forms due to film formation, scattering, and vehicle interactions.

e. Antioxidant Activity of *Syzygium myrtifolium* Extract

Antioxidant Activity Assay (DPPH Method):

The antioxidant activity of *Syzygium myrtifolium* extract was evaluated using the DPPH radical scavenging method [77,78].

- DPPH solution: 4 mg of 2,2-diphenyl-1-picrylhydrazyl (DPPH) was dissolved in 25 mL methanol p.a. to obtain a 160 ppm stock solution, stored in a dark bottle; Blank preparation: 0.3 mL of DPPH solution was diluted with methanol p.a. to 5 mL in a calibrated test tube; Extract stock solution: 25 mg of red shoot leaf extract was dissolved in methanol p.a. to yield a 1000 ppm solution; Serial dilutions: From the stock, extract solutions of 400, 500, 600, 700, and 800 ppm were prepared. For each concentration, 4.7 mL was mixed with 0.3 mL of DPPH solution in foil-wrapped test tubes.
- Standard comparison: A 1000 ppm vitamin C solution was prepared in methanol p.a. and protected from light.
- Absorbance was measured at 517 nm after incubation, and % inhibition was calculated to determine IC₅₀ values.

4.3.3. Synthesis of *Syzygium myrtifolium* Extract-Loaded Gelatin Nanoparticles

- Synthesis of Gelatin Nanoparticles via Precipitation Method [35,36]

a. Formulation Composition

Gelatin nanoparticles were formulated using red shoot leaf extract (300×IC₅₀), DMSO (0.2 mL), ethanol 96% (10 mL), Poloxamer 188 (700 mg), gelatin (5 mg), glutaraldehyde 2% (1 mL), and purified water (0.5 mL).

b. Solvent Phase

Gelatin (5 mg) was dissolved in 1 mL of purified water at 50 °C. Separately, red shoot leaf extract was dissolved in 0.2 mL DMSO and 0.2 mL ethanol 96%, stirred until homogeneous.

c. Non-Solvent Phase

Poloxamer 188 (700 mg) was dissolved in 10 mL ethanol 96% using a magnetic stirrer.

d. Nanoparticle Formation

The solvent phase was added dropwise into the non-solvent phase at 700 rpm. After 15 minutes, 0.5 mL glutaraldehyde was added, and stirring continued for 12 hours to complete crosslinking.

e. Purification and Drying

Nanoparticles were centrifuged at 700 rpm and washed three times with purified water (30 minutes each). The pellet was collected and freeze-dried for further use.

- Characterization of Gelatin Nanoparticles

a. Particle Size and Polydispersity Index (PDI) [35,36]

A 0.1 mL nanoparticle suspension was diluted to 10 mL with purified water. Particle size and PDI were measured using a Particle Size Analyzer, repeated three times.

b. Zeta Potential [35,36]

The same dilution protocol was used for zeta potential measurement using a Zeta Sizer, repeated three times.

c. Entrapment Efficiency (%EE) [35,36]

Six mg of nanoparticles were dissolved in 10 mL DMSO. Absorbance was measured at 202 nm using a UV-Vis spectrophotometer. Extract content was calculated using the linear regression equation ($y = a + bx$), and %EE was determined using:

- $$\%EE = (\text{Extract in nanoparticles} / \text{Initial extract}) \times 100\%$$

d. Morphology [76]
Surface morphology was examined using Scanning Electron Microscopy (SEM) to assess sphericity and aggregation tendency.

e. Functional Group Identification
Approximately 2 mg of sample was analyzed using Fourier Transform Infrared Spectroscopy (FTIR) to identify functional groups. [16]

f. Sun Protection Potential of SME-LG Nanoparticles
To assess the photoprotective potential, 10 mg of red shoot leaf extract was dissolved in 10 mL of 96% ethanol. Aliquots of 9.237 μL , 10.776 μL , and 12.388 μL —corresponding to $60\times\text{IC}_{50}$, $70\times\text{IC}_{50}$, and $80\times\text{IC}_{50}$ concentrations, respectively—were diluted to volume with ethanol and homogenized. The absorbance of each sample was measured using a UV-Vis spectrophotometer across the wavelength range of 290–320 nm.

The SPF value was calculated using the Mansur equation: [67]
where:

$$\text{SPF} = \text{CF} \times \sum (\text{EE}(\lambda) \times \text{I}(\lambda) \times \text{Abs}(\lambda))$$

SPF: Sun Protection Factor, the final measure of the sample's ability to protect against ultraviolet B (UVB) radiation, which is the primary cause of sunburn; CF: Correction Factor, a constant value typically set to 10; $\sum$ sum of: Summation symbol, indicating that the values are summed up across the relevant wavelength range; $\text{EE}(\lambda)$: Erythral Effect Spectrum at a specific wavelength (λ). This refers to the potential of UV radiation at that wavelength to cause skin redness or sunburn; $\text{I}(\lambda)$: Solar Intensity Spectrum at a specific wavelength (λ). This represents the intensity of the sun's radiation at that wavelength; $\text{Abs}(\lambda)$: Absorbance of the sample at a specific wavelength (λ). This value is measured using a UV-Vis spectrophotometer.

Moreover, SPF values can be expressed as percentage of UV blocking to make them more intuitive. The general approximation is: [68–70]

$$\% \text{ UV Blocking} = (1 - (1/\text{SPF})) \times 100.$$

- g. Antioxidant Activity of SME-LG Nanoparticles
The antioxidant activity of *Syzygium myrtifolium* extract was evaluated using the DPPH radical scavenging method [77,78]. As the standard comparison, a vitamin C solution was prepared in methanol p.a. and protected from light. Absorbance was measured at 517 nm after incubation, and % inhibition was calculated to determine IC_{50} values.

4.3.4. Preparation and Evaluations of Sunscreen Gel Formulations

- a. Preparation of Gel Formulation of *Syzygium myrtifolium* Extract
Two types of topical gel formulations were prepared using red shoot leaf extract (*Syzygium myrtifolium* Walp.): one with raw extract and the other with nanoparticle-loaded extract. Each formulation was designed to deliver antioxidant activity at concentrations equivalent to $300\times$, $600\times$, and $900\times$ the IC_{50} value obtained from the DPPH assay.

Table 19. Gel formulation containing *Syzygium myrtifolium* extract.

Ingredient	Blank	F I (300× IC ₅₀)	F II (600× IC ₅₀)	F III (900× IC ₅₀)
<i>Syzygium myrtifolium</i> extract	—	300× IC ₅₀	600× IC ₅₀	900× IC ₅₀
Carbomer 940	1	1	1	1
Propylene glycol	15	15	15	15
Phenoxyethanol	0.8	0.8	0.8	0.8
Triethanolamine	0.3	0.3	0.3	0.3
Green tea essence	qs	qs	qs	Qs
Purified water	ad 100 mL	ad 100 mL	ad 100 mL	ad 100 mL

Table 20. Gel formulation containing *Syzygium myrtifolium* extract-loaded nanoparticles (SME-LG NPs).

Ingredient	F I (300× IC ₅₀)	F II (600× IC ₅₀)	F III (900× IC ₅₀)
<i>Syzygium myrtifolium</i> extract	300× IC ₅₀	600× IC ₅₀	900× IC ₅₀
Carbomer 940	1	1	1
Propylene glycol	15	15	15
Phenoxyethanol	0.8	0.8	0.8
Triethanolamine	0.3	0.3	0.3
Green tea essence	qs	qs	Qs
Purified water	ad 100 mL	ad 100 mL	ad 100 mL

Note: Formulation F I (300× IC₅₀) was selected for further evaluation based on preliminary antioxidant calculations and optimal skin compatibility.

Procedures:

Red shoot leaf extract or its gelatin nanoparticles, Carbomer 940, glycerin, triethanolamine, phenoxyethanol, and purified water were weighed. Carbomer 940 was hydrated by dispersing it gradually into purified water (20× its weight) and left to swell for 24 h. The extract was dissolved in ethanol or dispersed in water, followed by the addition of phenoxyethanol and homogenization (Mixture 1). Swollen Carbomer 940 was stirred at 100 rpm and neutralized with triethanolamine (Mixture 2). Mixture 1 was incorporated into Mixture 2 under magnetic stirring, followed by green tea essence and incremental addition of the remaining water. The resulting gel was transferred into tubes and subjected to formulation evaluation, antioxidant activity assay, and sun protection factor (SPF) determination. [44–47]

b. Evaluation of Sunscreen Gel Formulations

Organoleptic, homogeneity, pH, viscosity, flowrate properties, and spreadability of sunscreen gel formulations were evaluated. [49–52]

c. Stability Evaluation of Gel Formulations

Stability testing was performed using the cycling test method, where gel samples were stored at 27 °C for 24 hours, followed by transfer to an oven at 40 °C for another 24 hours—constituting one cycle. A total of six cycles were conducted. Evaluations included organoleptic properties, pH, viscosity, spreadability, and homogeneity, along with SPF determination at week 0 and week 3. This approach aligns with current cosmetic stability guidelines, which emphasize stress testing under temperature fluctuations to simulate transport and storage conditions. [80]

- Organoleptic evaluation before and after cycling
- Homogeneity evaluation before and after cycling
- pH evaluation before and after cycling
- Viscosity before and after cycling
- Spreadability before and after cycling
- Formulation SPF before and after cycling
- Antioxidant activity of formulations before and after cycling

d. Franz Diffusion Profiles of Flavonoid Penetration

• Franz Diffusion Cell Procedure

Gel samples were tested using vertical Franz diffusion cells. A membrane (synthetic or excised skin) was mounted between the donor and receptor compartments. The receptor chamber was filled with phosphate buffer (pH 7.4) and maintained at 32 ± 1 °C with continuous stirring to ensure sink conditions.

A defined amount of gel (≈1–2 mg/cm²) was applied to the donor surface. Receptor fluid samples were withdrawn at predetermined intervals (e.g., 0.5–24 h) and replaced with fresh buffer. The permeated compound was quantified by UV–Vis or HPLC.

Permeation profiles were expressed as cumulative amount per unit area (μg/cm²) versus time, and flux (J) was calculated from the linear portion of the curve. The permeability coefficient (Kp) was determined by dividing flux by donor concentration.

- Preparation of Diffusion Membrane

The diffusion membrane was prepared using Whatman No. 1 filter paper, pre-soaked in a modified Spangler solution to simulate skin lipid composition. The Spangler solution consisted of: Coconut oil (15 g), oleic acid (15 g), white petrolatum (15 g), cholesterol (5 g), stearic acid (5 g), liquid paraffin (10 g), palmitic acid (10 g), and olive oil (25 g). The mixture was stirred until homogeneous, and the membrane was immersed for 15 minutes. The percentage of solution absorbed was calculated using:

$$\% \text{ Absorbed} = [(W_1 - W_0) / W_0] \times 100\%$$

where: (W_0), membrane weight before soaking; (W_1), membrane weight after soaking. This lipid-treated membrane was then mounted in the Franz diffusion cell for in vitro permeation studies.

- In Vitro Penetration and Sampling Protocol

The penetration study was conducted using a Franz diffusion cell. A synthetic membrane was positioned between the donor and receptor compartments. Approximately 1 g of sunscreen gel—either containing red shoot leaf extract or its gelatin nanoparticle formulation—was applied to the donor side of the membrane. The receptor compartment was filled with 16 mL phosphate buffer solution (pH 7.4) and maintained at $37 \pm 0.5^\circ \text{C}$ with continuous magnetic stirring at 250 rpm.

Aliquots of 3 mL were withdrawn from the receptor compartment at predetermined intervals (30, 60, 90, 120, 150, and 180 minutes) using a syringe. Each withdrawn volume was immediately replaced with an equal volume of fresh phosphate buffer (pH 7.4) to maintain sink conditions.

For phenolic content analysis, each sample was transferred to a vial and reacted with 80 μL Folin–Ciocalteu reagent. After 8 minutes, 0.6 mL of 7.5% sodium carbonate solution and phosphate buffer were added to reach the final volume. The mixture was incubated for 40–45 minutes at room temperature, and absorbance was measured at λ_{max} 710.6 nm using a UV-Vis spectrophotometer. [81] The cumulative amount of penetrated phenolic compound per unit membrane area was calculated using the following equation [82]:

$$Q = \frac{C_n \times V + \sum_{i=0}^{n-1} C_i \times S}{A}$$

where: Q is the cumulative penetrated amount ($\mu\text{g}/\text{cm}^2$), C_n is the phenol concentration at time point (n) ($\mu\text{g}/\text{mL}$), V is the volume of the Franz diffusion cell (mL), C_i is the concentration at each previous time point, S is the sampling volume (mL), and A is the membrane area (cm^2).

The penetration rate (flux) was determined using Fick's First Law [82]:

$$J = \frac{Q}{t}$$

where: J is the flux ($\mu\text{g}/\text{cm}^2/\text{min}$) and t is the elapsed time (min).

- Packaging

HDPE plastic tubes are highly durable, chemically resistant, and widely used in pharmaceutical, cosmetic, and industrial packaging due to their strength and safety profile. High-Density Polyethylene (HDPE) is a thermoplastic polymer derived from petroleum. It is known for its *high strength-to-density ratio*, *chemical resistance*, and *low moisture absorption*, making it ideal for packaging sensitive formulations.

Property: Mechanical strength, high tensile strength and impact resistance; Chemical resistance, inert to most acids, bases, and solvents; Moisture barrier, low water absorption, suitable for aqueous and semi-solid formulations; Thermal stability, operates safely in moderate temperature ranges; Biocompatibility, non-toxic and FDA-approved for food and pharmaceutical contact; and Recyclability, fully recyclable; marked as resin code #2. [83–85]

5. Patents

Not applicable

Author Contributions: Conceptualization, K.K. and E.M.; methodology, K.K., E.M. and W.C.; software, W.C.; validation, K.K., and E.M.; formal analysis, K.K., and E.M.; investigation, W.C.; resources, K.K.; data curation, K.K. and E.M.; writing—original draft preparation, W.C.; writing—review and editing, K.K and E.M.; visualization, W.C.; supervision, K.K. and E.M.; project administration, W.C.; funding acquisition, W.C. and K.K. All authors have read and agreed to the published version of the manuscript.

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