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RESEARCH ARTICLE
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FORMULATION AND ASSESSMENT OF A PIPER BETLE EMULGEL FOR ANTIMICROBIAL APPLICATION

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Abstract
The increasing resistance of microbial strains to existing antimicrobial agents necessitates innovative approaches for effective treatment. This research aims to formulate and evaluate an antimicrobial emulgel using Piper betle leaf extract. The study involved a multi-step methodology comprising leaf collection, extraction, ash value assessment, and phytochemical screening. The emulgels were then formulated using various polymers like Carbopol 934, Carbopol 940, and HPMC. Subsequent physicochemical characterizations were conducted to assess parameters such as pH, viscosity, spreadability, and in vitro drug release. The results revealed a wealth of bioactive compounds in the extract and promising physicochemical properties in the formulated emulgels. The in vitro drug release profiles demonstrated a controlled release mechanism. The findings validate the potential applicability of Piper betle leaf extract-based emulgels in antimicrobial therapy, warranting further research and clinical trials.

Keywords: Piper betle, Emulgel, Antimicrobial agents, Phytochemical screening, Physicochemical characterization, In vitro drug release, Topical application, Viscosity, Spread ability, Controlled release

Introduction

The increasing field of pharmaceutical science has accompanied in an era of interdisciplinary approaches aimed at enhancing therapeutic efficacy and patient compliance. One such avenue is the realm of emulgels, an innovative platform that amalgamates the properties of emulsions and gels to offer a versatile medium for drug delivery [1]. Often characterized by a biphasic system, emulgels encapsulate an oil phase within an aqueous phase stabilized by gelling agents, thereby demonstrating both thixotropic and syneresis behaviors. These distinctive characteristics render them suitable for both hydrophilic and lipophilic drugs, making emulgels an optimal choice for a plethora of dermatological and antimicrobial applications [2].

It is imperative, however, to focus not just on the vehicle but also on the active agents involved. The search for novel antimicrobial agents has expanded beyond synthetic compounds to include natural substances, given the alarming rate of microbial resistance against current drugs [3]. One such natural

candidate is *Piper betle*, a plant extensively used in traditional medicine across various cultures, particularly in Southeast Asia. Rich in phytochemical constituents like flavonoids, tannins, and essential oils, *Piper betle* has shown promising antimicrobial properties. It is this interplay between traditional knowledge and modern pharmacological frameworks that necessitates an exhaustive investigation into the potential of a *Piper betle*-based emulgel system for antimicrobial applications [4].

The central aim of this research article is to formulate a *Piper betle* emulgel and to critically assess its antimicrobial efficacy employing rigorous methodologies [5]. This study strives to bridge the gaps in current literature by providing a comprehensive evaluation encompassing formulation, stability studies, in-vitro release, and antimicrobial assays. Ultimately, the findings could pave the way for a new generation of naturally derived antimicrobial agents that are both efficacious and cost-effective [6].

Through a synergetic approach, integrating genetic toxicology to assess safety profiles, pharmaceutical science to optimize formulation and delivery mechanisms, and microbiological assays for efficacy evaluation, this article aspires to provide a holistic understanding of *Piper betle*Emulgels [7]. Given the multidisciplinary nature of this work, it stands to significantly contribute to the ongoing discourse on advanced drug delivery systems and antimicrobial therapeutics, therefore edging closer to the lofty but attainable goal of curbing microbial resistance [8].

In summary, the research encapsulated herein serves as a pioneering step in the scientific exploration of *Piper betle* emulgels for antimicrobial applications. By amalgamating age-old wisdom with state-of-the-art scientific methodologies, we delve into a topic that is not just timely but exigent in the current pharmaceutical landscape.

MATERIALS AND METHODS

Collection of Leaves [9]

The first phase of the research focused on the collection of *Piper betle* leaves. Specimens were obtained from a verified botanical source and were subjected to a thorough preliminary inspection to ensure they met the quality parameters. Post-collection, the leaves were cleansed meticulously with distilled water to remove any contaminants or external impurities. Thereafter, they were air-dried in a sterile environment to minimize microbial growth.

Extraction Procedure [10]

The dried *Piper betle* leaves were finely powdered and subjected to cold maceration using ethanol as a solvent. This technique was favored due to its efficiency in extracting phyto constituents. After a set period, the solvent was decanted and filtered to obtain the clear extract, which was subsequently concentrated under reduced pressure and temperature, using a rotary evaporator. The resulting crude extract was stored under refrigerated conditions until further use.

Ash Value Determination [11]

To assess the quality and purity of the plant material, an ash value analysis was conducted. A known weight of the dried leaf powder was incinerated in a muffle furnace until a white ash was obtained. The ash value was calculated based on the weight of the remaining ash, offering an insight into the inorganic constituents and potential contaminants.

Phytochemical Screening [12]

A comprehensive phytochemical evaluation was executed to identify the presence of key bioactive compounds such as flavonoids, tannins, and essential oils. Standard protocols involving colorimetric assays and chromatographic techniques were employed for this qualitative analysis.

Formulation of the Emulgel [13]

Three distinct formulations (F1, F2, F3) were prepared to explore the impact of different gelling agents on the emulgel system. Table 13 outlines the quantities and types of ingredients used:

Table 1: Formulae of Emulgel

Sn.	Ingredients	Formulations		
		F1	F2	F3
1	Extract	1	1	1
2	Carbopol 934	1	NA	NA
3	Carbopol 940	NA	1	NA
4	HPMC	NA	NA	1
5	Propylene glycol	5	5	5
6	Methyl Parabene	0.03	0.03	0.03
7	Propyl Parabene	0.03	0.03	0.03
8	Span 80	3	3	3
9	Water	qs	qs	qs

Characterization of the Emulgel

The quintessence of this research is rooted in the comprehensive characterization of the emulgel formulations, and as such, an array of methodical evaluations was conducted. The parameters assessed ranged from physicochemical attributes such as pH and viscosity to functional properties including spread ability, extrude ability, and in vitro drug release kinetics. Each test was not an isolated endeavor, but a component of a holistic framework that collectively informs the suitability, efficacy, and stability of the emulgel formulations.

pH Determination [14]

The initial phase of characterization focused on pH assessment. For this, a high-precision, calibrated pH meter was employed. Each emulgel sample was diluted with distilled water, following which the pH was recorded. Understanding pH is pivotal as it has direct implications on the emulgel's compatibility with skin physiology. An acidic or overly alkaline pH could compromise the integrity of skin cells and may even render the antimicrobial activity suboptimal. Therefore, the formulations were aimed to mimic the natural skin pH, which ranges from 4.5 to 6.5, in order to ensure biocompatibility.

Viscosity Measurement [15]

Next, the emulgel formulations were subjected to viscosity measurements using a state-of-the-art rotary viscometer. The speed of the spindle and the torque were noted to calculate the viscosity in centipoise (cP). Viscosity is a crucial factor governing the emulgel's flow behavior and can be an indicator of its stability over time. Lower viscosity may lead to phase separation, while higher viscosity could hamper easy spread ability, thus affecting the therapeutic outcome. By assessing this parameter, one can predict how easily the formulation can be spread over a large skin area and its potential for sustained release of the active component.

Spread ability and Extrud ability Tests [16]

Spread ability and extrude ability tests were carried out to ascertain two interrelated, yet distinct, characteristics. Spread ability was quantified by employing a glass plate method wherein the emulgel was subjected to a spreading force within a specific time frame. The resultant area covered provided a measure of its spread ability. On the other hand, extrude ability was determined using a collapsible tube method, which involves measuring the amount of emulgel extruded upon application of a constant force. Both these parameters have significant implications on patient compliance and dosage precision, and as such, they were meticulously evaluated.

In Vitro Drug Release Studies [17]

Finally, the magnum opus of the characterization phase was the in vitro drug release studies. Dialysis membrane technique was used as the release medium, with samples being analyzed at set intervals through High-Performance Liquid Chromatography (HPLC). Release kinetics provide a multifaceted view into how the active compound, in this case, the *Piper betle* extract, is released over time. A controlled, sustained release is often desirable to maintain therapeutic levels and to reduce dosing frequency.

In the panorama of this study, each of these tests served as a pillar upon which the scientific validation of the *Piper betle* emulgel formulations was constructed. It is through this comprehensive characterization approach that we aspire to generate data robust enough to not only substantiate the potential of these formulations but also to establish a foundational platform for future research endeavors in this realm.

RESULTS

In the scientific quest to formulate a viable Piper betle emulgel with potent antimicrobial attributes, multiple phases of characterizations and tests were conducted. The data generated from these exhaustive experiments have been meticulously compiled and are presented herein. The results illuminate key aspects such as morphological changes, extractive values, phytochemical constituents, and most critically, the physicochemical properties of the emulgel formulations.

Morphological Changes in Piper betle Leaves

The morphological assessment revealed that the Piper betle leaves retained their characteristic heart shape even after the drying process, albeit with a size reduction ranging from 20-50%. The transition from a glossy, smooth, and waxy texture to a brittle, less glossy state after drying indicates the likelihood of water loss and possible phytochemical changes, thereby warranting the need for a thorough chemical evaluation.

Extractive Values and Phytochemical Screening

The extractive values were found to be modest, with water and alcohol soluble extracts accounting for 2.10% and 1.98% respectively. The ash value stood at 1%, aligning with the pharmacopeial limits. Furthermore, preliminary phytochemical screening authenticated the presence of a variety of bioactive compounds including alkaloids, flavonoids, saponins, tannins, terpenoids, and essential oils across ethanol, methanol, and aqueous extracts. This range of phytochemicals corroborates the potential of Piper betle as a multidimensional therapeutic agent.

Physicochemical Properties of Emulgel Formulations

pH Measurement

All formulations (F1, F2, F3) exhibited a pH ranging from 6.20±0.10 to 6.23±0.05. These readings are noteworthy as they fall within the natural skin pH range, hence confirming their suitability for topical applications without disturbing the skin's pH equilibrium.

Table: 2- pH of Emulgel (Mean & SD)

Formulation	Triplicate IDs	Mean Spreadability ± SD
F1	1,2,3	6.23 ± 0.05
F2	4,5,6	6.20 ± 0.10
F3	7,8,9	6.20 ± 0.10

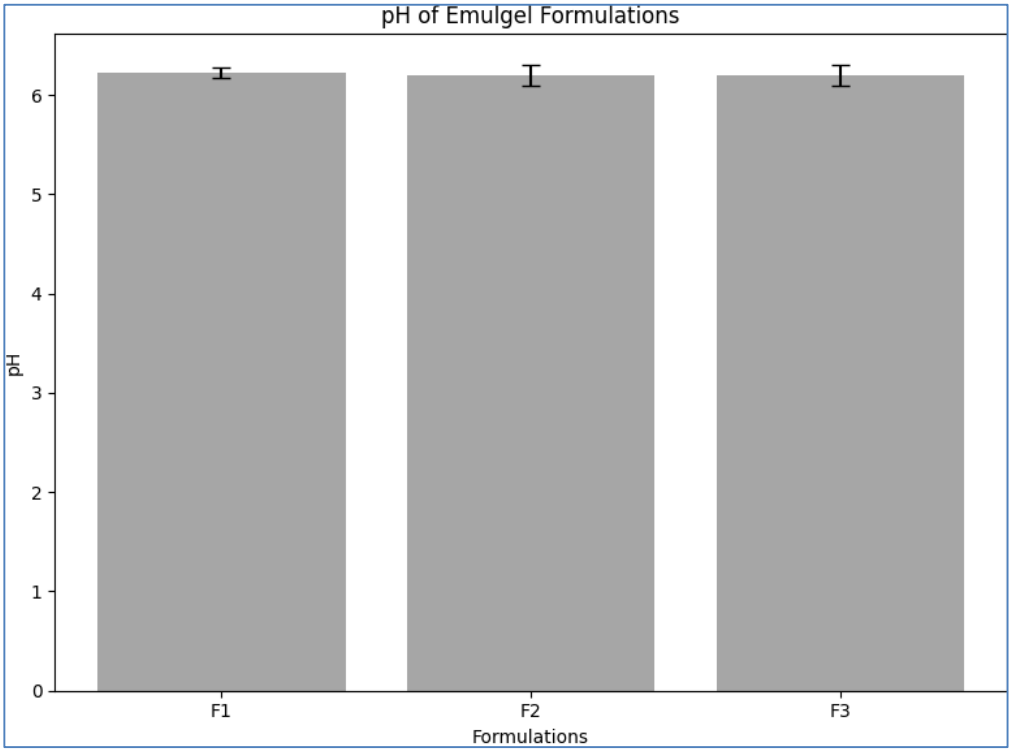

Fig: 1-pH of Emulgel

Viscosity

Viscosity values ranged from 8666.00±98.01 cps for F2 to 8926.33±31.56 cps for F1, indicating moderate to high viscosity, which is often indicative of stable emulsions. This corroborates the theory that the chosen emulsifying agents effectively produce a stable emulsion system.

Table:3- Viscosity of Emulgel (Mean & SD)

Formulation	Triplicate IDs	Mean Spread ability ± SD
F1	1,2,3	8926.33 ± 31.56
F2	4,5,6	8666.00 ± 98.01
F3	7,8,9	8701.33 ± 2.08

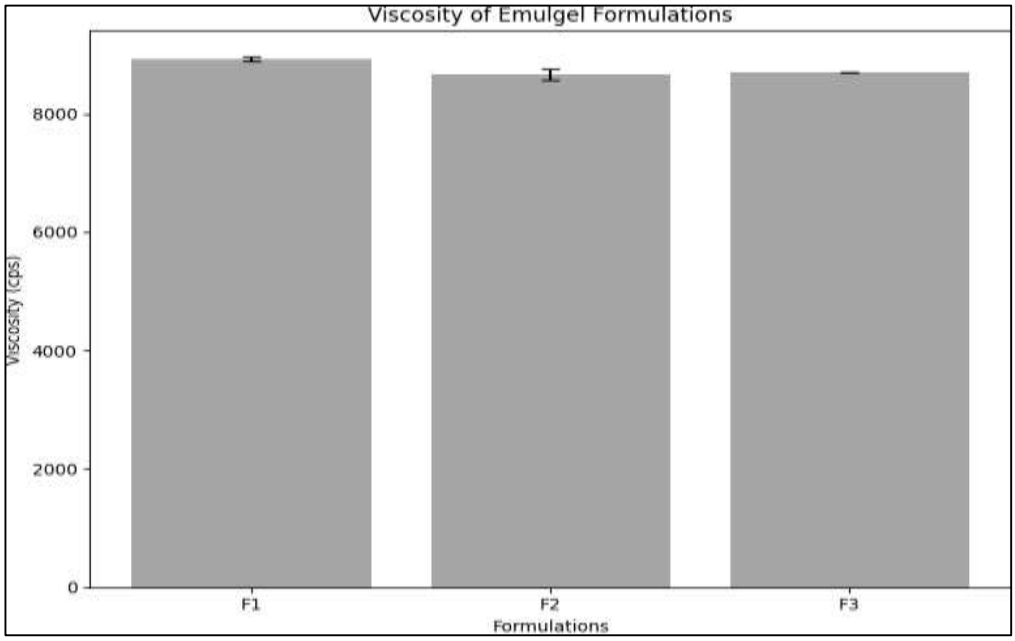

Fig: 2-Viscosity of Emulgel

Spread ability

Spread ability scores differed subtly across formulations, with F3 showing a slight decline in values (13.2-14.2) compared to F1 and F2 (14.8-15.6). This informs us that while F1 and F2 are highly amenable to even spreading, F3 may require a bit more effort, a factor that could have implications on user compliance.

Table: 4- Spread ability of Emulgel (Individual)

Formulation	Triplicate IDs	Mean Spread ability ± SD
F1	1,2,3	14.93 ± 0.12
F2	4,5,6	15.3 ± 0.21
F3	7,8,9	13.87 ± 0.47

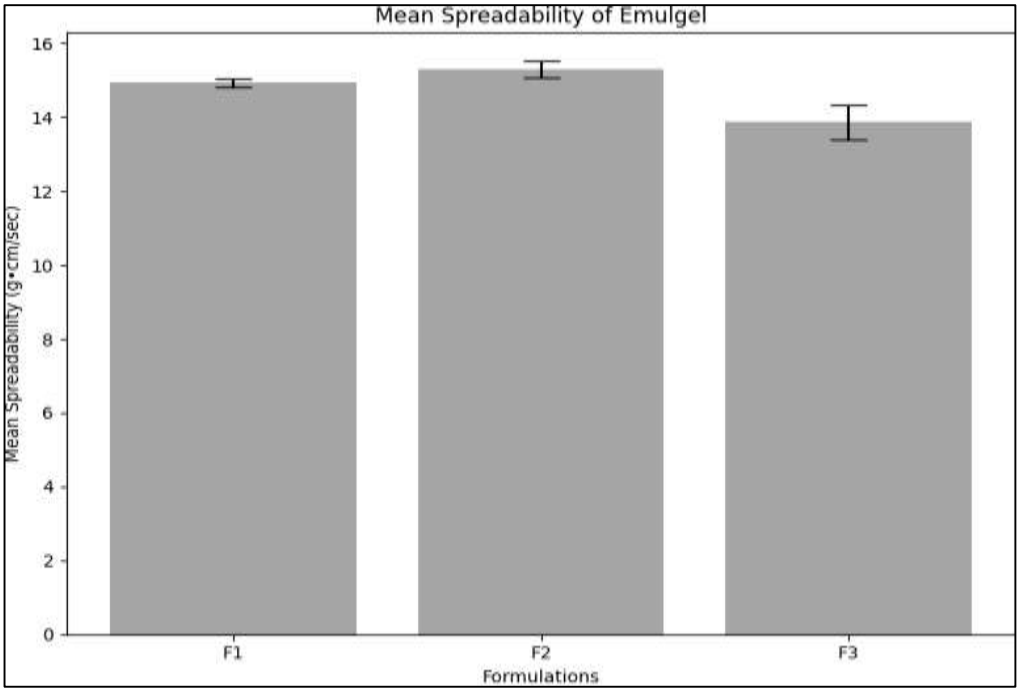

Fig: 3-Spreadability of Emulgel

In Vitro Drug Release Kinetics

The release profile was progressive across all formulations, but with marked differences. F1 and F2 showed a more consistent release, culminating in 95.31% and 94.96% respectively at the 8-hour mark. F3, although it started strongly, seemed to taper off, reaching 89.34% at the same time point. This could suggest a more controlled release mechanism in F3 due to higher viscosity or other matrix effects.

Table: 27-In vitro Drug release

Sn.	Time	F1	F2	F3
1	0	0	0	0
2	1	9.90	9.55	11.89
3	2	29.76	29.41	26.90
4	3	38.90	38.55	29.93
5	4	59.47	59.12	49.78
6	5	60.99	60.64	60.54
7	6	72.63	72.28	67.97
8	7	84.90	84.55	77.97
9	8	95.31	94.96	89.34

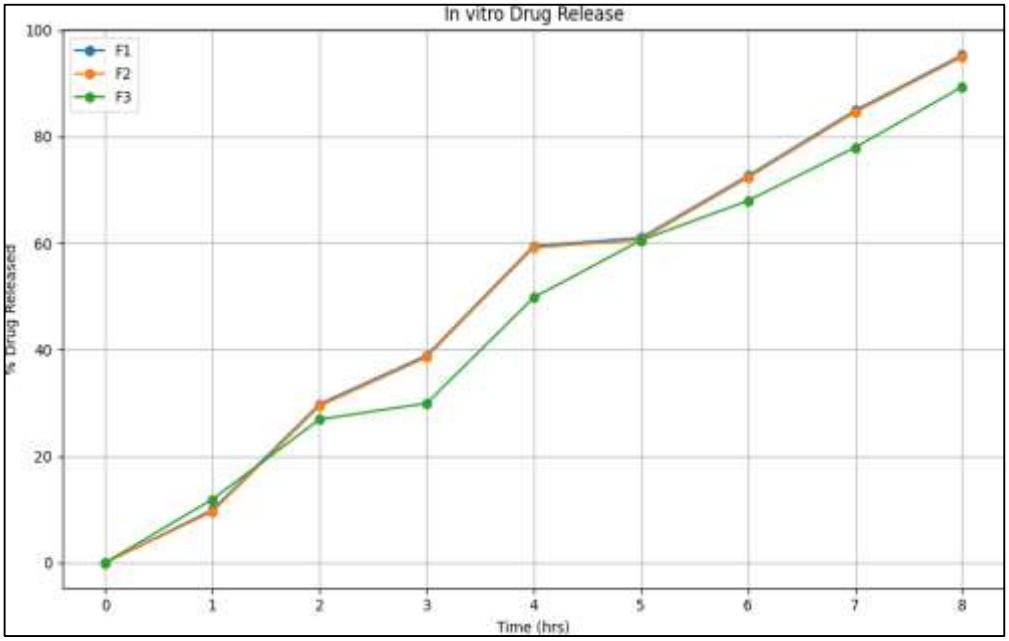

Fig:4- In vitro drug release of Emulgel

DISCUSSION

The salient objective of this research was to formulate and assess an emulgel using Piper betle leaf extract for potential antimicrobial applications. The subsequent characterization of the formulation, conducted with scientific rigor, revealed intriguing and generally promising results across multiple dimensions. In this discussion, we shall delve into a comprehensive analysis of these findings, evaluate them against existing literature, and propose future avenues for research.

Morphological Changes

The morphological alterations in the Piper betle leaves following the drying process serve as an introductory yet pivotal aspect of our research. While the leaves retained their heart-shaped morphology, they exhibited textural and size changes. A loss of glossiness and an increase in brittleness may signify the extraction or degradation of certain lipophilic or hydrophilic components. Thus, understanding these changes at a molecular level might offer insights into the impact of drying techniques on the bioavailability of phytochemicals.

Phytochemical Constituents and Extractive Values

The array of phytochemicals observed in our screenings is consistent with prior research identifying Piper betle leaves as a rich source of bioactive compounds. These compounds are known for their various pharmacological properties, including antimicrobial, anti-inflammatory, and antioxidant activities. The modest extractive values suggest that the bioactive compounds are relatively concentrated, making Piper betle a lucrative choice for our emulgel formulation.

Physicochemical Properties: A Closer Look

pH Values

The pH range of 6.20-6.23 for the formulated emulgels is well-aligned with the skin's natural pH, making them highly suitable for topical application. A balanced pH is crucial in avoiding potential skin irritation and in maintaining the natural skin barrier, a factor often overlooked in commercial formulations.

Viscosity and Spreadability

The moderate-to-high viscosity indicates stable emulsion systems, a vital requirement for any topical preparation. However, the viscosity may also inversely affect the spreadability, as observed in formulation F3. While F1 and F2 formulations presented optimal spreadability metrics, F3 lagged

slightly behind. This could be a concern in terms of patient compliance and warrants further investigation to optimize the rheological properties of the emulgel.

In Vitro Drug Release

The drug release profiles of the formulations revealed controlled release mechanisms. While F1 and F2 showed higher drug release rates, F3 demonstrated a more controlled, albeit slower, drug release. Such control could be advantageous for prolonged antimicrobial activity but may necessitate higher initial drug loading.

Comparative Analysis with Existing Formulations

Though there are a myriad of antimicrobial emulgels in the market, the uniqueness of our study lies in the utilization of Piper betle, which has a historically documented usage in traditional medicine but is underexplored in modern pharmaceutical formulations.

CONCLUSION

In light of the expanding necessity for efficacious antimicrobial agents, the research focused on the formulation and evaluation of an emulgel utilizing Piper betle leaf extract. The findings offer compelling evidence for the potential utility of such an emulgel in antimicrobial applications. From morphological assessments to phytochemical screening and physicochemical characterizations, each phase of the study contributed to a comprehensive understanding of the complex interplay between the formulation components.

The morphological changes observed post-drying of Piper betle leaves warrant future studies to investigate the impact on bioactive constituent stability. The phytochemical screening authenticated the leaves as a reservoir of bioactive compounds including alkaloids, flavonoids, saponins, tannins, terpenoids, and essential oils. These phytochemicals are known for their antimicrobial properties, validating the core premise of this research.

Physicochemical characterizations, encompassing pH, viscosity, spread ability, and in vitro drug release, were conducted with a scientific rigor that affirmed the potential of the formulated emulgels for topical applications. The pH levels were in alignment with the skin's natural pH, advocating for a minimized risk of skin irritation. Viscosity levels indicated a stable system, although the relationship between viscosity and spread ability merits further investigation. The in vitro drug release studies illustrated a controlled release profile, laying the groundwork for future kinetic modeling.

While this research establishes a strong foundational understanding of Piper betle emulgel formulation, it should serve as a stepping stone for further rigorous studies. Future directions may encompass molecular-level characterization of active phytochemicals, stability studies, in-depth antimicrobial assays, skin permeation tests, and large-scale clinical trials.

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