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Development of Anti-acne Gel Containing Combination of Pineapple Extract and Berberine Extract

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ABSTRACT:

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit that predominantly affects adolescents and young adults, with a global prevalence of approximately 85% among individuals aged 12–24 years [1,2]. The condition is characterized by the formation of comedones, papules, pustules, and nodules resulting from increased sebum production, follicular hyperkeratinization, microbial colonization, and inflammation [3,4]. The colonization of Cutibacterium acnes plays a crucial role in acne pathogenesis by inducing inflammatory mediators and immune responses [5]. Conventional therapies such as antibiotics, retinoids, and benzoyl peroxide are effective but associated with adverse effects such as irritation, dryness, and antibiotic resistance [6,7].

Herbal formulations have gained attention due to their safety and effectiveness [8]. The present study focuses on a herbal anti-acne gel containing pineapple extract (bromelain) and berberine extract. Bromelain exhibits anti-inflammatory and wound-healing properties [9], while berberine shows strong antibacterial and anti-inflammatory activity [10]. The formulated gel was evaluated for physicochemical properties and showed promising results with good stability and minimal irritation [34]. Thus, the formulation can be considered a safe and effective alternative for acne management.

KEYWORDS:

Acne vulgaris, Herbal gel, Pineapple extract, Bromelain, Berberine, Anti-inflammatory, Antibacterial, Carbopol gel, Topical formulation, Skin irritation, Drug content uniformity, Spreadability, Herbal dermatology, Natural anti-acne treatment, Cutibacterium acnes.

INTRODUCTION :

1.1 Structure and Functions of Skin

The skin is the largest organ of the human body and serves as a protective barrier against environmental factors such as microorganisms, ultraviolet radiation, and toxins [12]. It also plays an important role in thermoregulation and immune defense [12]. Structurally, the skin consists of the epidermis, dermis, and hypodermis, each contributing to its protective and physiological functions [13]. The pilosebaceous unit, which includes sebaceous glands and hair follicles, is primarily involved in acne development [1].

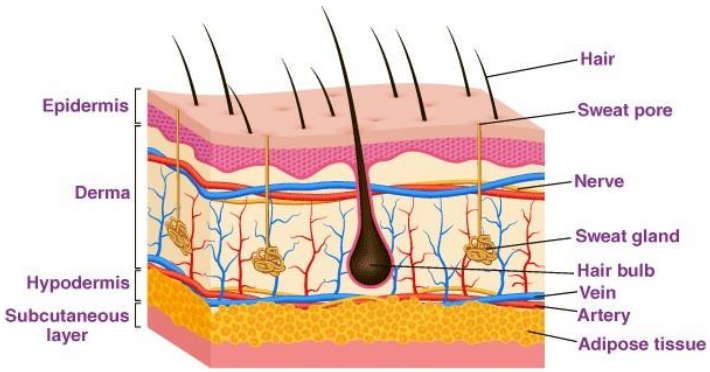

Figure 1 : Structure of Skin

1.2 Overview of Acne Vulgaris

Definition and General Description

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit, which comprises the hair follicle, sebaceous gland, and associated structures [1]. It is one of the most prevalent dermatological conditions worldwide and primarily affects adolescents, although it can persist into adulthood or even appear later in life [2]. The disorder is characterized by a variety of lesions including non-inflammatory lesions such as comedones (blackheads and whiteheads) and inflammatory lesions such as papules, pustules, nodules, and cysts [3]. These lesions commonly appear on areas rich in sebaceous glands, including the face, chest, shoulders, and upper back [14].

Acne is not merely a cosmetic concern but a medical condition with potential physical and psychological consequences. Severe acne can lead to permanent scarring and pigmentation, while even mild forms may significantly affect an individual's quality of life [15].

Figure 2 : Acne Vulgaris

Epidemiology

Acne vulgaris affects approximately 85% of adolescents between the ages of 12 and 24 years, making it one of the most common skin disorders globally [2]. It is observed in both males and females, although males often experience more severe forms due to higher androgen levels [14]. Adult acne, particularly in women, has also been increasingly reported, often associated with hormonal imbalances and lifestyle factors [6].

The prevalence and severity of acne vary depending on genetic, environmental, and lifestyle factors. Urban populations tend to have higher incidence rates due to dietary habits, stress, and exposure to pollution [8]. Despite its high prevalence, acne is often under-treated due to lack of awareness or fear of side effects from conventional treatments [6].

Types of Acne Lesions

Acne lesions are broadly classified into non-inflammatory and inflammatory types based on their clinical presentation [3].

Non-inflammatory lesions include open comedones (blackheads), which are characterized by oxidized melanin giving a dark appearance, and closed comedones (whiteheads), which appear as small, flesh-colored bumps [19]. These lesions result from blockage of hair follicles by sebum and keratin.

Inflammatory lesions include papules, pustules, nodules, and cysts, which are associated with redness, swelling, and pain [3]. These lesions occur due to bacterial colonization and immune response within the follicle [24]. Severe forms such as nodulocystic acne can lead to scarring and require aggressive treatment [6].

Pathophysiology of Acne

The pathogenesis of acne is multifactorial and involves four major mechanisms: increased sebum production, follicular hyperkeratinization, microbial colonization, and inflammation [3,4].

Sebum production is stimulated by androgens, particularly during puberty, leading to enlargement of sebaceous glands and increased lipid secretion [14]. This excess sebum combines with dead skin cells, resulting in blockage of hair follicles and formation of comedones [19].

Follicular hyperkeratinization refers to abnormal shedding of keratinocytes within the follicle, which contributes to obstruction and accumulation of sebum [4]. This creates an

ideal environment for the growth of Cutibacterium acnes, an anaerobic bacterium implicated in acne development [5].

The bacterium metabolizes sebum into free fatty acids, which irritate the follicular wall and trigger inflammation [21]. It also activates immune responses by stimulating toll-like receptors, leading to the release of cytokines such as interleukin-1 and tumor necrosis factor-alpha [22]. These inflammatory mediators contribute to the formation of papules and pustules [24].

Recent studies suggest that inflammation may occur even before visible lesion formation, indicating its primary role in acne pathogenesis [25]. Oxidative stress further aggravates inflammation and tissue damage, worsening acne severity [26].

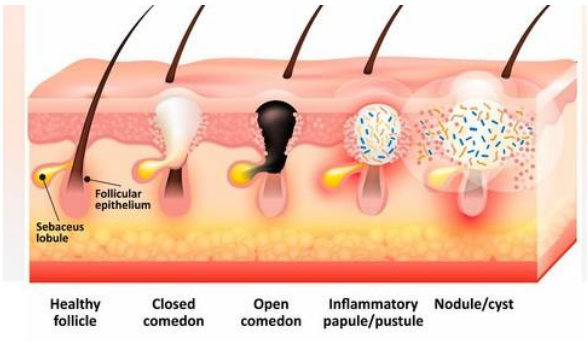

Figure 3 : Pathophysiology of Acne

Factors Affecting Acne

Several internal and external factors influence the development and severity of acne [6]. Hormonal changes are the primary factor, particularly during puberty, menstruation, and pregnancy, where increased androgen levels stimulate sebum production [14]. Genetic predisposition also plays a role, as individuals with a family history of acne are more likely to develop the condition [6].

Dietary factors, especially consumption of high glycemic index foods and dairy products, have been associated with increased acne severity due to their effect on insulin and hormonal pathways [20]. Stress is another contributing factor, as it increases cortisol levels, leading to increased sebum production and inflammation [6].

Environmental factors such as pollution, humidity, and use of comedogenic cosmetics can clog pores and worsen acne [8]. Poor skincare practices and excessive use of oily products may also contribute to acne development.

Psychological Impact of Acne

Although acne is not life-threatening, it can have significant psychological effects, particularly among adolescents and young adults [15]. Individuals with acne often

experience low self-esteem, social anxiety, and depression due to their appearance [15]. Severe acne and scarring can lead to long-term emotional distress and reduced quality of life. Studies have shown that the psychological burden of acne can be comparable to that of chronic diseases such as asthma and diabetes [15]. Therefore, effective management of acne is important not only for physical health but also for mental well-being.

Need for Effective Treatment

The increasing prevalence of acne and its associated complications highlight the need for effective and safe treatment options [6]. Conventional therapies such as antibiotics and retinoids are widely used but are associated with side effects like irritation, dryness, and antibiotic resistance [6,7].

These limitations have led to a growing interest in alternative approaches, particularly herbal formulations, which offer multi-targeted action with fewer side effects [8].

Herbal treatments provide antimicrobial, anti-inflammatory, and antioxidant effects, making them suitable for long-term use [16]. The use of natural ingredients such as bromelain and berberine offers a promising approach to acne management by targeting multiple pathogenic factors simultaneously.

1.3 Limitations of Conventional Therapy

Overview

Conventional treatments for acne include topical and systemic therapies such as antibiotics, retinoids, benzoyl peroxide, and hormonal agents [6]. While these treatments are effective, they are associated with several limitations and adverse effects.

Side Effects

Conventional treatments for acne include topical and systemic therapies such as antibiotics, retinoids, benzoyl peroxide, and hormonal agents [6]. While these treatments are effective, they are associated with several limitations and adverse effects.

Antibiotic Resistance

Long-term use of antibiotics can lead to the development of resistant strains of Cutibacterium acnes, reducing treatment effectiveness [6]. This has become a major concern in dermatological practice.

Recurrence of Acne

Acne often recurs after discontinuation of treatment, indicating that conventional therapies do not provide a permanent solution [6]. This highlights the need for alternative approaches.

1.4 Herbal Approach in Acne Management

Importance of Herbal Medicine

Herbal medicines have gained popularity due to their safety, effectiveness, and minimal side effects [8]. They contain bioactive compounds such as flavonoids, alkaloids, and phenolics that exhibit antimicrobial and anti-inflammatory properties [16].

Advantages of Herbal Formulations

Herbal formulations provide multi-targeted action by addressing different aspects of acne pathogenesis simultaneously [16]. They are suitable for long-term use and reduce the risk of adverse effects associated with synthetic drugs [8].

1.5 Pineapple Extract

Introduction

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Chemical Composition

Bromelain is not a single compound but a mixture of proteolytic enzymes along with other components such as phosphatases, glucosidases, peroxidases, and cellulases [30]. It also contains trace amounts of carbohydrates and minerals that contribute to its stability and activity [30]. The enzymatic activity of bromelain is highly dependent on pH and temperature, with optimal activity observed in slightly acidic to neutral conditions, making it suitable for skin applications [9].

Anti-inflammatory Activity

One of the most important properties of bromelain is its anti-inflammatory effect. It inhibits the synthesis of pro-inflammatory mediators such as prostaglandins and cytokines, thereby reducing inflammation [30]. It also modulates the immune response by decreasing neutrophil migration to inflamed tissues [31]. This activity is particularly beneficial in acne, where inflammation plays a major role in lesion formation [3]. By reducing inflammation,

bromelain helps in minimizing redness, swelling, and discomfort associated with acne lesions.

Keratolytic and Exfoliating Action

Bromelain exhibits keratolytic activity by breaking down keratin, a structural protein present in the outer layer of the skin [31]. This helps in removing dead skin cells and unclogging pores, thereby preventing the formation of comedones [19]. The exfoliating action of bromelain promotes smoother skin texture and enhances the penetration of other active ingredients into the skin [31]. This property makes it highly suitable for inclusion in topical anti-acne formulations.

Wound Healing and Skin Regeneration

Bromelain has been reported to promote wound healing by enhancing tissue regeneration and reducing inflammation at the site of injury [30]. It increases collagen synthesis and accelerates the repair of damaged skin, which is particularly useful in reducing acne scars [31]. Its ability to remove necrotic tissue without damaging healthy cells further contributes to faster healing.

Antimicrobial Activity

Although primarily known for its anti-inflammatory properties, bromelain also exhibits mild antimicrobial activity against certain bacteria [9]. It enhances the effectiveness of other antimicrobial agents by increasing their penetration into tissues [30]. This synergistic effect is beneficial when used in combination with antibacterial agents such as berberine.

Role in Anti-Acne Formulation

The incorporation of bromelain in anti-acne formulations provides multiple benefits, including reduction of inflammation, removal of dead skin cells, and promotion of healing [9]. Its enzymatic activity helps in maintaining clear pores and preventing acne formation. Additionally, its natural origin ensures minimal side effects, making it suitable for long-term use [8].

Figure 4 : Pineapple

1.6 Berberine Extract

Introduction

Berberine is a naturally occurring isoquinoline alkaloid found in several medicinal plants such as Berberis vulgaris [10]. It has been widely used in traditional medicine for its antimicrobial, anti- inflammatory, and metabolic regulatory properties [10]. In recent years, berberine has gained attention in dermatology for its potential role in acne treatment.

Chemical Nature and Properties

Berberine is a yellow-colored alkaloid with a bitter taste and is soluble in water and alcohol [10]. Its chemical structure allows it to interact with various biological pathways, contributing to its wide range of pharmacological effects [33]. It exhibits good stability under normal conditions, making it suitable for formulation in topical preparations [36].

Antibacterial Activity

One of the most significant properties of berberine is its strong antibacterial activity against Cutibacterium acnes [32]. It disrupts bacterial cell membranes and interferes with DNA replication, leading to inhibition of bacterial growth [32]. Berberine also prevents biofilm formation, which is a major factor in antibiotic resistance [23]. This makes it an effective alternative to conventional antibiotics used in acne treatment.

Anti-inflammatory Activity

Berberine exhibits potent anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines such as interleukins and tumor necrosis factor-alpha [10]. It also reduces oxidative stress by scavenging free radicals, thereby preventing tissue damage [26]. These properties help in reducing redness, swelling, and pain associated with acne lesions.

Sebum Regulation

Excess sebum production is a major factor in acne development, and berberine has been shown to regulate lipid metabolism and reduce sebum secretion [33]. It acts on sebaceous glands and hormonal pathways to control oil production, thereby preventing pore blockage and acne formation [14].

Antioxidant Properties

Berberine possesses strong antioxidant activity, which helps in neutralizing free radicals and reducing oxidative stress in the skin [26]. This protects skin cells from damage and supports overall skin health. Antioxidants play an important role in preventing inflammation and aging- related skin issues.

Role in Anti-Acne Formulation

Berberine is highly effective in anti-acne formulations due to its combined antibacterial, anti- inflammatory, and sebum-regulating properties [10]. It directly targets the major causes of acne and enhances the overall effectiveness of the formulation. When combined with bromelain, it provides a synergistic effect, improving therapeutic outcomes [9,10].

Figure 5 : Berberine

LITERATURE REVIEW:

Martins, Ferreira, and Barros (2022) reviewed the therapeutic potential of herbal products in dermatology and reported that plant-derived bioactive compounds possess antimicrobial, antioxidant, anti-inflammatory, and wound-healing properties. Their findings support the growing application of herbal ingredients in the management of chronic skin disorders, including acne vulgaris.

Sharma, Verma, and Gupta (2021) developed a polyherbal anti-acne gel and reported significant therapeutic efficacy with minimal skin irritation. The study concluded that combining multiple herbal ingredients can enhance anti-acne activity through synergistic mechanisms.

Patel, Patel, and Shah (2020) formulated and evaluated herbal topical gels and observed favorable physicochemical characteristics such as suitable pH, good spreadability,

stability, and user acceptability. Their findings confirmed the suitability of Carbopol-based gels for herbal drug delivery.

Wang et al. (2020) investigated the antibacterial properties of berberine and reported strong inhibitory activity against several pathogenic microorganisms. The study demonstrated that berberine disrupts bacterial cell membranes and suppresses microbial proliferation, indicating its potential as a natural antimicrobial agent for acne treatment.

Mukherjee (2019) highlighted the increasing popularity of herbal medicines due to their safety, efficacy, and reduced incidence of adverse effects compared with synthetic drugs. The author also emphasized the importance of standardization and quality control in herbal product development.

Imenshahidi and Hosseinzadeh (2019) reviewed the pharmacological activities of berberine and reported its antimicrobial, anti-inflammatory, antioxidant, and metabolic regulatory effects. Their findings suggested that berberine may be beneficial in the management of various inflammatory disorders, including acne vulgaris.

Coenye, Peeters, and Nelis (2018) highlighted the significance of bacterial biofilms in acne pathogenesis and treatment resistance. The authors emphasized that agents capable of inhibiting biofilm formation may improve acne management, making berberine an attractive therapeutic candidate due to its antibiofilm properties.

Zaenglein et al. (2016) developed evidence-based clinical guidelines for acne management and highlighted growing concerns regarding antibiotic resistance associated with prolonged antibiotic use. The authors stressed the importance of identifying safer and more sustainable alternatives to conventional antibiotic therapy.

Del Rosso (2016) discussed recent advances in acne pathophysiology and treatment. The study emphasized that successful acne management should address multiple pathogenic factors simultaneously, including microbial proliferation, inflammation, sebum overproduction, and follicular hyperkeratinization.

RESEARCH METHODOLOGY:

Materials

S.no	Materials Required	Quantity Taken	Use
1	Pineapple extract	2%	Active ingredient
2	Berberine extract	1%	Active ingredient
3	Carbopol 940	1%	Used to form the gel base
4	Glycerine	5%	Keeps skin hydrated and improves texture
5	Propylene glycol	5%	Attracts and retains moisture in the skin
6	Methyl paraben	0.2%	Prevent microbial growth
7	Propyl paraben	0.02%	Prevent microbial growth
8	Triethanolamine	q.s	Adjusts pH and helps in gel formation
9	Distilled water	q.s	For dissolving extracts, if required)
10	Beaker	2	Used to prepare and mix the formulation
11	Glass rod	1	Used for manual stirring and mixing
12	Pipette	1	Used to measure and transfer small volumes of liquids
13	Measuring cylinder	1	Used to measure larger volumes of liquids

Formulation of Herbal Anti-Acne Gel

The herbal anti-acne gel was prepared using the Carbopol gel base method [17]. Carbopol 940 was accurately weighed and dispersed in distilled water and allowed to hydrate for 24 hours to ensure complete swelling and proper gel formation [17]. After hydration, propylene glycol was added as a humectant and penetration enhancer, followed by the addition of methylparaben as a preservative [36].The prepared pineapple extract and berberine extract were then incorporated into the gel base with continuous stirring to ensure uniform distribution of active ingredients [34]. The pH of the formulation was adjusted using triethanolamine, which also facilitated gel formation [17]. The mixture was stirred until a homogeneous gel was obtained and stored in suitable containers for further evaluation [34].

Figure 6 : Formulated Gel

Determination of pH

The pH of the formulated herbal anti-acne gel was determined using a calibrated digital pH meter to ensure its compatibility with skin pH [37]. Initially, the pH meter was standardized using buffer solutions of known pH (4.0, 7.0, and 9.0) to ensure accuracy of measurement [37]. A small quantity of the gel was taken and dispersed in distilled water to obtain a uniform solution [36]. The electrode of the pH meter was then immersed into the prepared gel dispersion, and the reading was recorded once the value stabilized [37]. The procedure was repeated multiple times to ensure reproducibility and reliability of the measurement [38]. Proper cleaning of the electrode with distilled water was carried out between measurements to avoid contamination [37].

Spreadability Test

Spreadability of the gel was determined to evaluate the ease of application on the skin surface [17]. A known quantity of gel was placed between two clean glass slides of uniform size [34]. A specific weight was placed on the upper slide to allow the gel to spread uniformly between the slides [17]. After a fixed time interval, the diameter of the spread gel was measured or the time required for separation of slides under applied weight was recorded [34]. The experiment was performed under controlled conditions to maintain consistency [36]. This method helps in determining the extent to which the gel can be easily applied over the affected area [17].

Drug Content Uniformity

Drug content uniformity was determined using UV-visible spectrophotometry to assess the distribution of active ingredients in the gel [40]. A known quantity of gel was accurately weighed and dissolved in a suitable solvent such as methanol or distilled water to extract the active components [36]. The solution was filtered using Whatman filter paper to remove any undissolved particles [40]. The filtrate was then diluted appropriately to obtain a measurable concentration [40]. The absorbance of the prepared solution was measured at specific wavelengths corresponding to bromelain and berberine using a UV spectrophotometer [40]. The experiment was repeated to ensure accuracy and reproducibility [38]. The method ensures that the active ingredients are uniformly distributed throughout the formulation [36].

Skin Irritation Test

The skin irritation test was conducted to evaluate the safety of the formulation for topical application [39]. A small quantity of the gel was applied to a specific area of the skin, usually

on the forearm or behind the ear, under controlled conditions [39]. The applied area was observed at regular intervals for any signs of irritation such as redness, itching, swelling, or burning sensation [39]. The test was conducted over a specified duration to assess both immediate and delayed reactions [39]. Proper ethical considerations and precautions were followed during the test [36]. This method helps in determining the compatibility of the formulation with skin [39].

Physical Appearance

The physical appearance of the gel was evaluated by visual inspection to assess parameters such as color, texture, homogeneity, and presence of any particulate matter [34]. A small quantity of gel was observed under normal light conditions [36]. The formulation was checked for uniformity and absence of lumps or phase separation [34]. The consistency and smoothness were also evaluated by manual inspection [17]. This evaluation ensures that the formulation is aesthetically acceptable and suitable for application [36].

Stability Studies

Stability studies were conducted to evaluate the physical and chemical stability of the formulation under different environmental conditions [36]. The gel samples were stored in suitable containers and subjected to various conditions such as room temperature, refrigeration, and elevated temperature [36]. The samples were observed periodically for changes in color, consistency, pH, and phase separation [36]. Stability testing helps in determining the shelf life and storage conditions of the formulation [36].

DISCUSSION/SUGGESTIONS:

Overview of Evaluation Results

The formulated herbal anti-acne gel was evaluated for various physicochemical parameters to determine its suitability, stability, and effectiveness for topical application [36]. The results obtained from pH determination, spreadability, drug content uniformity, skin irritation test, and physical appearance confirmed that the formulation met the required standards for dermatological preparations [34].

pH Analysis

The pH of the formulation was measured using a digital pH meter, and the test was performed three times to ensure accuracy and reproducibility [37,38]. The average pH was found to be 6.0, which lies within the normal physiological range of skin pH (5.5–7.0) [3]. This indicates that the formulation is suitable for topical application without causing irritation or disruption of the skin barrier [3]. Maintaining an appropriate pH is essential for preserving skin integrity and ensuring stability of active ingredients [36].

S.no	Trial	pH Value
1	Trial 1	6.0
2	Trial 2	6.0
3	Trial 3	6.0
	Average	6.0

Figure 7.1: List of trials of pH Determination

Figure 7.2 : pH Determination

Spreadability Study

The spreadability of the gel was tested on different skin types and was found to be good. This indicates that the formulation can be easily applied over the skin surface with minimal effort [17]. Good spreadability ensures uniform distribution of active ingredients and enhances their penetration into the skin [34]. It also improves patient compliance, as formulations that spread easily are more acceptable for regular use [17]. The presence of

Carbopol as a gelling agent contributed to achieving an optimal balance between viscosity and spreadability [36].

Figure 8 : Spreadability Test

Drug Content Uniformity

Drug content uniformity was evaluated using UV spectrophotometry, and the test was performed three times to ensure consistency [40]. The absorbance value obtained was 0.482, which falls within the acceptable range of 0.4–0.9, indicating uniform distribution of active ingredients within the gel [40]. The absorbance range for pineapple extract was found to be 0.2–0.6, while for berberine it ranged from 0.486, confirming the presence of both active components in appropriate concentrations [10].

S.no	Trial	Absorbance
1	Trial 1	0.484
2	Trial 2	0.486
3	Trial 3	0.486
	Average	0.486

Figure 9.1: List of trials of Absorbance Determination

Figure 9.2: Drug Absorbance Graph

Skin Irritation Test

The skin irritation test showed that no irritation, redness, or itching was observed upon application of the gel [39]. This indicates that the formulation is safe and well-tolerated by the skin. The absence of irritation can be attributed to the use of natural ingredients and maintenance of skin- compatible pH [8]. This result confirms that the formulation is suitable for topical use and can be safely applied for acne treatment [39].

Physical Appearance

The prepared gel was yellow in color, which is attributed to the presence of pineapple extract and berberine [9,10]. The formulation exhibited a smooth texture, good homogeneity, and absence of lumps or phase separation [34]. Aesthetic properties such as color and texture play an important role in user acceptance and compliance [17]. The observed physical characteristics indicate that the formulation is stable and suitable for application [36].

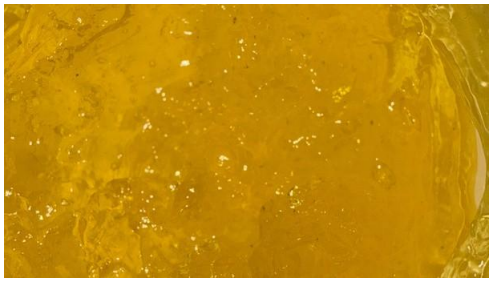

Figure 10 : Physical Appearance of Formulated Gel

CONCLUSION:

The evaluation results indicate that the formulated herbal anti-acne gel possesses suitable physicochemical properties for topical application [36]. The pH of the gel was found to be 6.0, which lies within the normal skin pH range (5.5–7.0), ensuring compatibility and minimizing the risk of irritation [3]. Maintaining appropriate pH is essential for preserving the skin barrier and stability of the formulation [37].

The gel exhibited good spreadability, indicating ease of application and uniform distribution of active ingredients over the skin surface [17]. This property enhances patient compliance and therapeutic effectiveness. The optimized concentration and proper hydration of Carbopol contributed to achieving the desired consistency and spreadability [36].

Drug content uniformity was confirmed by UV spectrophotometric analysis, with an absorbance value of 0.482 falling within the acceptable range (0.4–0.9) [40]. This indicates uniform distribution of pineapple extract and berberine in the formulation, ensuring consistent therapeutic activity [36]. The 24-hour hydration of Carbopol played a key role in

achieving homogeneity [17]. The skin irritation test showed no signs of irritation, redness, or itching, confirming the safety of the formulation for topical use [39]. This is an advantage over conventional treatments, which often cause side effects [6]. The physical appearance of the gel was smooth, homogeneous, and light yellow in color, indicating stability and good aesthetic quality [34].

Overall, the formulation demonstrated stability, safety, and effectiveness, making it a promising herbal alternative for acne treatment due to the combined anti-inflammatory and antibacterial action of bromelain and berberine [9,10].

CONFLICT OF INTEREST:

This paper is based on a conceptual review of published literature and does not involve direct funding or collaboration with commercial biotechnology entities. The author declares no financial or personal conflicts of interest related to the subject matter discussed.

REFERENCES:

1. Zaenglein AL, Pathy AL, Schlosser BJ, et al. (2016). Guidelines of care for the management of acne vulgaris. Journal of the American Academy of Dermatology.
2. Tan JK, Bhate K. (2015). A global perspective on the epidemiology of acne. British Journal of Dermatology.
3. Gollnick HP. (2003). From new findings in acne pathogenesis to new approaches in treatment. Current Medical Research and Opinion.
4. Kligman AM. (1974). An overview of acne. Journal of Investigative Dermatology.
5. Dessinioti C, Katsambas A. (2010). The role of Propionibacterium acnes in acne pathogenesis. Journal of the European Academy of Dermatology and Venereology.
6. Thiboutot D, Gollnick H, Bettoli V, et al. (2009). New insights into the management of acne. Journal of the American Academy of Dermatology.
7. Zaenglein AL. (2016). Acne vulgaris treatment guidelines. Journal of the American Academy of Dermatology.
8. Mukherjee PK. (2019). Quality Control of Herbal Drugs. Elsevier.
9. Pavan R, Jain S, Kumar A. (2012). Properties and therapeutic application of bromelain: A review. Biomedical Reports.
10. Imenshahidi M, Hosseinzadeh H. (2019). Pharmacological effects of berberine. Phytotherapy Research.
11. Gaur M, Sharma N, Singh P. (2024). Herbal formulations in dermatology. International Journal of Pharmaceutical Sciences.
12. Proksch E, Brandner JM, Jensen JM. (2008). The skin: an indispensable barrier. Experimental Dermatology.
13. Madison KC. (2003). Barrier function of the skin. Journal of Investigative Dermatology. 14.Zouboulis CC. (2004). Acne and sebaceous gland function. Clinics in Dermatology.
14. Williams HC, Dellavalle RP, Garner S. (2012). Acne vulgaris. The Lancet.
15. Martins N, Ferreira ICFR, Barros L. (2022). Herbal products in dermatology. Phytotherapy Research.
16. Swarbrick J. (2007). Encyclopedia of Pharmaceutical Technology. Informa Healthcare.
17. Del Rosso JQ. (2016). Advances in acne pathophysiology. Journal of Clinical and Aesthetic Dermatology.
18. Pappas A. (2009). The relationship of diet and acne. Dermato-Endocrinology.
19. Smith RN, Mann NJ, Braue A, et al. (2007). Low glycemic-load diet in acne. American Journal of Clinical Nutrition.
20. Grice EA, Segre JA. (2011). The skin microbiome. Nature Reviews Microbiology. 22.Kim J. (2005). Review of the innate immune response in acne. Dermatology.

21. Coenye T, Peeters E, Nelis HJ. (2018). Biofilm formation in acne. Journal of Applied Microbiology.
22. Kurokawa I, Danby FW, Ju Q, et al. (2009). New developments in acne inflammation. Experimental Dermatology.
23. Jeremy AH, Holland DB, Roberts SG, et al. (2003). Inflammatory events in acne. Journal of Investigative Dermatology.
24. Bowe WP, Logan AC. (2010). Acne vulgaris and oxidative stress. Journal of Drugs in Dermatology.
25. Enshaieh S, Jooya A, Siadat AH, et al. (2007). Efficacy of tea tree oil in acne. Indian Journal of Dermatology.
26. Surjushe A, Vasani R, Saple DG. (2008). Aloe vera: A short review. Indian Journal of Dermatology.
27. Mahmood T, Akhtar N, Khan BA. (2010). Green tea and skin health. Pakistan Journal of Pharmaceutical Sciences.
28. Maurer HR. (2001). Bromelain: Biochemistry and medical use. Cellular and Molecular Life Sciences.
29. Fitzhugh DJ, Shan S, Dewhirst MW, et al. (2008). Bromelain treatment effects. Planta Medica.
30. Wang Y, Liu Y, Du X, et al. (2020). Antibacterial activity of berberine. Frontiers in Microbiology.
31. Kong W, Wei J, Abidi P, et al. (2004). Berberine and lipid metabolism. Nature Medicine.
32. Patel D, Patel N, Shah V. (2020). Formulation and evaluation of herbal gel. International Journal of Pharmaceutical Sciences Review and Research.
33. Sharma P, Verma N, Gupta R. (2021). Polyherbal anti-acne gel study. Journal of Pharmaceutical Research.
34. Aulton ME. (2013). Aulton's Pharmaceutics: The Design and Manufacture of Medicines. Elsevier.
35. Lachman L, Lieberman HA, Kanig JL. (2009). The Theory and Practice of Industrial Pharmacy. CBS Publishers.
36. Montgomery DC. (2017). Design and Analysis of Experiments. Wiley.
37. Barel AO, Paye M, Maibach HI. (2009). Handbook of Cosmetic Science and Technology. CRC Press.
38. Beckett AH, Stenlake JB. (2001). Practical Pharmaceutical Chemistry. CBS Publishers