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Development and Evaluation of a Polyherbal Neem-Based Emulgel Enriched with Herbal Oils for Enhanced Topical Delivery and Antibacterial Efficacy

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KEYWORDS

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ABSTRACT:

Introduction: The rising demand for natural and safe dermatological treatments has renewed interest in herbal formulations, particularly those utilizing Azadirachta indica (neem). However, poor solubility and permeability limit its direct application. Emulgels, combining the benefits of emulsions and gels, offer an innovative solution for enhanced topical delivery. Neem (Azadirachta indica), with its well-documented antimicrobial and wound-healing properties but poor solubility, presents an ideal candidate for emulgel formulation when combined with synergistic essential oils (clove, jasmine, rose).

Objective: This study aimed to develop and characterize a stable neem-based polyherbal emulgel enriched with clove, jasmine, and rose oils for improved antibacterial efficacy, stability, and patient acceptability that overcomes neem's solubility limitations while enhancing therapeutic efficacy against common skin pathogens (E. coli and S. aureus) and improving wound healing parameters.

Methods: Neem extract was obtained via Soxhlet extraction and characterized through phytochemical and FTIR analysis. Neem extract was incorporated into an emulgel with Carbopol 934, guar gum, and essential oils. Emulgel formulations were prepared and evaluated for organoleptic properties, rheological characteristics (viscosity: 1050 cP, spreadability: 26.3 g.cm/sec), pH (5.0), stability, and antimicrobial efficacy via disc/well diffusion assays. Antibacterial Testing performed with disc and agar well diffusion methods against Escherichia coli and Staphylococcus aureus were performed. Skin irritancy was assessed through 24-hour patch tests on human volunteers.

Journal of Chemical Health Risks

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Results: The emulgel exhibited optimal pH (5.0), viscosity (1050 cP), and spreadability (26.3 g·cm/s) with no phase separation. FTIR confirmed retention of bioactive compounds (e.g., nimbidin, eugenol). Antibacterial activity: Zones of inhibition ranged from 19–25.5 mm, comparable to gentamicin (30 mm). Non-irritating: Patch tests showed excellent skin compatibility. The optimized formulation demonstrated excellent antibacterial activity (25.5 mm zone against E. coli, 21 mm against S. aureus), representing 75-85% of gentamicin's efficacy. FTIR confirmed retention of bioactive functional groups (C=O at 1723 cm^{-1}, O-H at 3334 cm^{-1}). The emulgel showed no irritation in human tests and maintained stability under various storage conditions.

Conclusion: The neem-based emulgel successfully combines traditional herbal knowledge with modern drug delivery technology, offering a safe, effective natural alternative to synthetic topical antimicrobials with broad-spectrum activity and excellent patient acceptability.

1. INTRODUCTION

The growing preference for natural therapeutics has driven significant advancements in topical drug delivery systems, with emulgels emerging as innovative hybrid formulations that combine the benefits of emulsions and gels.[1-3] These systems offer superior drug loading capacity, enhanced stability, and controlled release properties, making them particularly valuable for dermatological applications. Their unique biphasic structure enables effective delivery of both hydrophilic and lipophilic compounds while maintaining excellent rheological properties, addressing key challenges in herbal formulation development.[4-7]

Neem (Azadirachta indica) has been a cornerstone of traditional medicine systems like Ayurveda for over two millennia, valued for its potent antibacterial, antifungal, anti-inflammatory, and wound-healing properties.[8,9] The bioactive compounds in neem, including nimbidin and azadirachtin, contribute to its therapeutic efficacy in treating various skin conditions. However, the plant's poor solubility and permeability limit its direct application, necessitating advanced delivery systems like emulgels to enhance bioavailability and therapeutic outcomes through improved solubilization, skin penetration, and controlled release mechanisms.[10,11]

The integration of multiple herbs in emulgel formulations creates synergistic effects that enhance therapeutic efficacy. Complementary essential oils such as clove, with its antimicrobial eugenol content, jasmine for skin hydration, and rose for antioxidant protection, work together with neem to address modern dermatological needs. This polyherbal approach aligns with traditional medicine principles while offering comprehensive solutions for conditions like acne and dermatitis, combining the benefits of multiple active compounds in a single formulation.[12-15]

The therapeutic validation of this formulation will examine its superior physicochemical stability and spreadability compared to conventional gels, along with enhanced antibacterial efficacy against common pathogens. Wound healing parameters such as epithelialization and collagen deposition will be evaluated, alongside assessments of patient acceptability focusing on texture and irritation potential. The study methodology incorporates systematic evaluation of delivery system performance through release kinetics and stability testing under various conditions.[16,17]

Therapeutic outcomes will be measured through microbial assays for antibacterial activity and histopathological analysis for wound healing effects. Safety and compliance studies will examine skin

Journal of Chemical Health Risks

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JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

irritation potential and user acceptability to ensure the formulation meets both therapeutic and cosmetic expectations. This multifaceted approach to evaluation ensures a comprehensive understanding of the emulgel's performance and potential applications.[18,19]

By merging traditional herbal knowledge with modern pharmaceutical technology, this research seeks to establish a natural alternative to synthetic topical antimicrobials. The neem-based emulgel is anticipated to demonstrate enhanced therapeutic potential through improved solubility, penetration, and controlled release of bioactive compounds. Its multifunctional design addresses infection, inflammation, and tissue repair simultaneously, while maintaining a patient-centric focus on cosmetic appeal and ease of use.[20,21]

Emulgels represent an innovative hybrid drug delivery system that combines the advantageous properties of both emulsions and gels, creating a versatile platform for topical administration of both hydrophilic and lipophilic drugs.[22,23] Their unique biphasic composition enables effective delivery of diverse therapeutic agents while offering superior drug loading capacity, enhanced stability, and controlled release characteristics compared to conventional topical formulations. These systems exhibit excellent spreadability, a non-greasy texture, and thixotropic behavior, along with aesthetic advantages such as being visually appealing and typically odorless, contributing to improved patient compliance.[23] The manufacturing process for emulgels involves several key steps as represented in **Figure 1**: first, the oil phase is prepared by dissolving lipophilic components in appropriate oils; simultaneously, the aqueous phase is created by hydrating gelling agents in water; these two phases are then combined to form a stable emulsion using suitable emulsifying agents; finally, the emulsion is incorporated into a gel base to create the final emulgel product. This relatively simple and cost-effective process requires no specialized equipment yet yields formulations capable of bypassing first-pass metabolism for targeted delivery with reduced systemic effects. While emulgels offer numerous benefits including efficient solubilization of various drug types and optimized release profiles, they do present certain limitations such as potential skin irritation in sensitive individuals and variable absorption of larger molecules, necessitating careful formulation design and testing to maximize therapeutic efficacy while minimizing adverse effects. The non-occlusive nature of emulgels avoids the greasy residue associated with many traditional formulations, further enhancing their patient acceptability and making them particularly valuable for dermatological applications requiring both cosmetic elegance and therapeutic performance.[24,25]

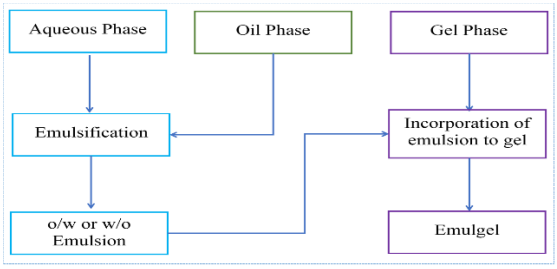

Figure 1: Diagrammatic Depiction of the Steps Involved in the Creation of Emulgel

Neem (Azadirachta indica)

Azadirachta indica, commonly known as Margosa tree, Indian neem, or Arishtha, is derived from the dried leaves, seeds, and bark of the plant belonging to the Meliaceae family. Primarily found in tropical and subtropical regions, including India, Bangladesh, Pakistan, and Nepal, neem exhibits distinct organoleptic properties characterized by its bitter taste and pigmentation due to carotenoids, chlorophyll a, and chlorophyll b. The plant contains numerous bioactive constituents, such as azadirachtin, alkaloids (nimbin, salannin, nimbidin), quercetin, isoprenoids, non-isoprenoids (proteins, carbohydrates), coumarin, tannins, sulfurous compounds, and polyphenolics, including flavonoids and their glycosides. These compounds contribute to neem's broad-spectrum medicinal properties, demonstrating anti-inflammatory, anti-arthritic, antipyretic, hypoglycemic, anti-ulcer, antifungal, antibacterial,

Journal of Chemical Health Risks

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JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

and anticancer activities, making it a valuable resource in traditional and modern therapeutics.[26-30]

Clove (Syzygium aromaticum)

Clove, also known as clove buds or clove flowers, consists of the dried flower buds of Eugenia caryophyllus, a member of the Myrtaceae family. Indigenous to Indonesia, it is widely cultivated in regions including Zanzibar, Pemba, Brazil, Amboiana, Sumatra, Madagascar, Penang, Mauritius, the West Indies, India, and Ceylon. The buds are characterized by their intensely pungent aroma and sultry sweet flavor, attributed to their high eugenol content (60–90% of the 14–21% volatile oil present). Additional bioactive constituents include acetyl eugenol, gallotannic acid, α- and β-caryophyllenes, methyl furfural, gum, resin, fiber, and caryophyllin. Medicinally, clove exhibits broad-spectrum antimicrobial activity against fungi and bacteria, and serves as an antiseptic, stimulant, carminative, and flavoring agent. Its applications extend to pain relief (anodyne), antiemetic effects, and oral anesthesia, particularly in root canal treatments. Clove oil is traditionally used to alleviate toothache, prevent vomiting, and address gastrointestinal disorders like diarrhea and intestinal worms. Eugenol, its primary bioactive compound, is employed as a local anesthetic in minimal doses, while cloves are also reputed for their aphrodisiac properties.[31-34]

Jasmine (Jasminum officinale)

Jasmine, known by various names including Arabian jasmine, Indian jasmine, Sampaguita, and Mogra, is derived from the flowers, leaves, and essential oil of Jasminum officinale, belonging to the Oleaceae family. This fragrant plant is commercially cultivated across India, Thailand, China, and the Philippines, characterized by its distinctive white flowers that emit a sweet, pungent aroma and exhibit nyctinastic movement, opening at night and closing during daylight hours. Phytochemical analysis reveals the presence of valuable constituents including alkaloids, flavonoids, phenols, tannins, saponins, and terpenoids, with specific compounds such as quercetin, rutin, gallic acid, and kaempferol identified in extracts. Traditional medicinal applications span multiple therapeutic areas, where jasmine serves as an antidepressant, analgesic, sedative, anti-inflammatory, antiseptic, expectorant, and aphrodisiac. Ethnomedical practices employ its roots for wound healing and snake bite treatment, while in South China it's used to manage hepatitis and diabetes. In Western Himalayan regions, it finds application against urinary tract infections and as a mild sedative, anxiolytic, astringent, and analgesic agent. Contemporary research supports its antioxidant, anti-inflammatory, and anti-diabetic properties, with additional uses in mood enhancement, anxiety relief, and digestive complaints, underscoring its versatility in both traditional and modern therapeutic systems.[36-40]

Rose (Rosa indica / Rosa damascena)

Commonly known as Damask Rose or Damascena Rose, Rosa damascena is a flowering plant from the Rosaceae family, characterized by its vibrant pink and red blossoms. Indigenous to Iran, this species is now primarily cultivated in Bulgaria and Turkey for commercial purposes. The plant displays distinctive organoleptic features, with large, fragrant flowers and odd-pinnate leaves typically consisting of 5-7 leaflets. Its rich phytochemical composition includes terpenes, glycosides, flavonoids, anthocyanins, carboxylic acids, myrcene, vitamin C, kaempferol, and quercetin, while its essential oil contains valuable compounds such as β-citronellol, nonadecane, geraniol, nerol, and additional kaempferol. Therapeutically, Damask Rose demonstrates remarkable versatility, exhibiting hypnotic, anticonvulsant, and antidepressant properties, along with significant anti-anxiety and analgesic effects. Its medicinal applications extend to respiratory benefits as an antitussive and bronchodilator, while also demonstrating anti-inflammatory, antimicrobial, and even anti-HIV potential. Additional therapeutic uses include managing diabetes through its anti-diabetic activity, providing antioxidant protection, serving as a cardiovascular stimulant, and offering anti-aging benefits. The plant also finds application in

Journal of Chemical Health Risks

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ophthalmic treatments and as a gentle laxative, making it a valuable resource in both traditional and modern pharmacopeias.[41-43]

This study aims to develop and evaluate a neem-based polyherbal emulgel with specific research objectives focused on creating a stable, cosmetically acceptable topical product. The formulation combines neem extract with carefully selected essential oils to harness their complementary therapeutic actions. Comprehensive evaluation will assess physicochemical properties including pH, viscosity, and spreadability, along with drug content uniformity and in vitro release kinetics to ensure optimal performance.

This work contributes significantly to the field of herbal pharmaceutics by developing a scientifically validated, stable, and effective topical delivery system. The formulation meets contemporary therapeutic demands while preserving the holistic principles of traditional medicine, offering a promising solution for natural skincare that bridges ancient wisdom with modern scientific rigor. The expected outcomes include an optimized delivery system that maximizes the therapeutic potential of neem and complementary herbs, providing a safe and effective alternative to conventional treatments.

2. Research Objectives

This study aims to develop and evaluate a novel polyherbal emulgel formulation incorporating Azadirachta indica (neem) extract combined with selected essential oils for enhanced topical delivery and therapeutic efficacy. The primary objectives focus on:

- ✓ Formulation Development: Designing a stable emulgel system that combines neem's bioactive compounds (nimbidin, azadirachtin) with synergistic herbal oils (clove, jasmine, rose) to improve solubility, skin permeation, and antibacterial activity.
- ✓ Physicochemical Characterization: Systematically evaluating critical parameters including viscosity, pH, spreadability, and stability to ensure optimal performance and patient acceptability.
- ✓ Therapeutic Assessment: Investigating the formulation's antibacterial efficacy against common skin pathogens (Escherichia coli, Staphylococcus aureus) through in vitro assays, comparing its potency to standard treatments.
- ✓ Safety Profiling: Conducting skin irritation studies to validate biocompatibility for topical application.
- ✓ Technology Integration: Leveraging the emulgel's dual emulsion-gel matrix to overcome neem's inherent limitations (poor solubility, permeability) while preserving its anti-inflammatory, antioxidant, and wound-healing properties.

By merging traditional herbal medicine with advanced drug delivery technology, this research seeks to establish a natural, cost-effective alternative to synthetic topical agents for managing dermatological conditions.

3. Materials and Methods

3.1. Materials

The formulation components were carefully selected from reputable suppliers to ensure quality and consistency. Industrial-grade neem powder served as the primary active ingredient, sourced from Research Lab Chemicals along with other key components including Carbopol 934 gelling agent, sodium alginate, and guar gum. Essential oils - rose oil, clove oil, and jasmine oil - were obtained from Yucca Enterprises for their therapeutic properties. Various laboratory-grade excipients such as methyl paraben (preservative), NaOH (pH adjuster), EDTA (chelating agent), polysorbate 80 (emulsifier), cetyl alcohol (emollient), and liquid paraffin (moisturizer) were all procured from Research Lab Chemicals. Methanol, used for extraction purposes, was also acquired as an industrial-grade solvent from the same supplier. This selection of materials from established manufacturers ensured the formulation met pharmaceutical standards while maintaining the desired therapeutic profile.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

3.2 Extraction of neem extract using Soxhlet apparatus

The Soxhlet apparatus was selected for its superior extraction efficiency, particularly for heat-stable phytochemicals. The system consists of three key components: a 500 mL round-bottom flask (Borosilicate glass), a Soxhlet extractor (40-60 µm porosity thimble), and a Liebig condenser (300 mm jacket length). This configuration enables continuous cyclic extraction through solvent reflux, ensuring exhaustive phytochemical recovery. Fresh neem leaves (Azadirachta indica) were shade-dried at 38±2°C for 72 hours, then pulverized using an electric grinder (500 µm particle size) to maximize surface area. 75 g of powdered neem was loaded into an extraction thimble, placed in the Soxhlet chamber. 800 mL of 96% ethanol (pharmaceutical grade) was added to the round-bottom flask. The assembly was heated at 70°C using a thermostatically controlled heating mantle. Each extraction cycle (15-20 minutes duration) continued automatically for 8 hours, allowing Solvent evaporation → condensation → percolation through sample → siphon return. The ethanol extract was concentrated using a rotary evaporator (40°C, 100 rpm, 175 mbar), yielding a dark green semisolid (22-25% w/w). The concentrate was stored in amber glass vials at 4°C until formulation.[44-46]

3.3 Evaluation of Neem Extract

3.3.1 Organoleptic Evaluation

The physical characteristics of neem extract were examined by observing its color, texture, odor, and appearance under normal light. The extract exhibited a dark green to brown hue and had a strong, distinctive smell, which is typical of neem-based preparations.[47,48]

3.3.2 Phytochemical Screening

A series of qualitative tests were conducted to identify key bioactive compounds in the extract. For phenols, a few drops of ferric chloride solution were added, resulting in a deep blue-green color. Alkaloids were detected using Dragendorff's reagent, which produced an orange-red precipitate. Tannins were confirmed by a blackish-green color upon reaction with ferric chloride, while saponins were identified by persistent foam formation when the extract was shaken with water. Additionally, the Keller-Killiani test revealed the presence of glycosides through the formation of a brown ring at the interface of the test solution.[49,50]

3.3.3 Solubility Studies

The extract's solubility was tested in different solvents, including water, ethanol, propylene glycol, and various oils. When mixed and agitated, neem extract showed partial solubility in water, ethanol, and propylene glycol but dissolved more effectively in oils such as eucalyptus, clove, jasmine, and rose oil.[49,50]

3.3.4 pH Determination

To ensure compatibility with topical application, the pH of a 1% neem extract solution was measured using a calibrated pH meter. The recorded pH fell within the acceptable range of 5.5 to 6.5, making it suitable for skin use without causing irritation. These evaluations confirm the extract's physicochemical stability and functional properties for formulation into dermatological products.[49,50]

3.3.5 Stability Study

Under two conditions i.e. room temperature (25°C ± 2°C, 60% RH) and desiccator storage neem extract was investigated for physical stability over 14 days. Whereas the desiccator storage reduced moisture exposure, the extract at room temperature stayed exposed to ambient humidity and temperature variations. Under normal lighting, observations on Day 7 and Day 14 were noted with an eye toward color and scent changes. Two storage environments were compared in order to evaluate any variations.[49,50]

3.4 Selection of Ingredients

The formulation incorporates Azadirachta indica (neem) as the primary active pharmaceutical ingredient (API) due to its multifaceted therapeutic properties. Rich in bioactive compounds like nimbidin

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

and azadirachtin, neem extract delivers potent antibacterial, anti-inflammatory, and wound-healing effects, effectively targeting acne, skin infections, and promoting tissue regeneration while providing antioxidant protection against oxidative damage. This action is synergistically enhanced by clove oil, whose high eugenol content contributes strong analgesic, antifungal, and antibacterial properties that accelerate skin repair, reduce inflammation, and prevent microbial growth.[51,52]

To optimize skin compatibility and sensory attributes, jasmine oil was included for its exceptional moisturizing and skin-conditioning capabilities, which enhance hydration and improve elasticity while offering mild antibacterial protection. Rose oil complements this system with its dual anti-inflammatory and antioxidant activities, helping to calm irritation, stimulate cell turnover, and maintain skin barrier function, while its aromatic profile improves user acceptability. The structural foundation utilizes Carbopol 934 as the primary gelling agent, selected for its superior thickening capacity and controlled release properties that ensure prolonged therapeutic action. Guar gum acts as a natural stabilizer, preventing phase separation and enhancing viscosity, while sodium alginate improves film formation for better hydration and sustained active ingredient absorption.[53,54]

The formulation's stability and texture are further refined by key excipients: EDTA chelates metal ions to enhance preservative efficacy and shelf life; liquid paraffin and cetyl alcohol work synergistically as emollients to create a protective moisture barrier and provide a smooth, creamy consistency; and Tween 80 ensures optimal emulsification for uniform dispersion of oil and water phases. Together, these carefully selected components create a stable, multifunctional emulgel that effectively delivers therapeutic benefits while maintaining excellent cosmetic appeal and skin tolerability.

3.5 Drug-excipient compatibility (FTIR)

The absorption wavelengths observed in the sample provide qualitative information about the specific chemical groups present in the analyzed material. For quantitative analysis, the absorption intensity at characteristic wavelengths correlates with the concentration of the corresponding chemical functional groups. This non-destructive analytical technique offers simplicity in operation and is applicable to both organic and inorganic compounds. The FTIR spectral data was acquired using a SHIMADZU spectrometer operating in the 4000-400 cm-1 range, with samples analyzed directly without pretreatment. Spectral data processing was performed using JASCO Spectra Manager II software. The measurement parameters included 45 scans per sample at a resolution of 2 cm-1 to ensure high-quality spectral data acquisition. Both the neem extract and its derived formulations were subjected to identical analytical conditions for consistent comparative analysis.[55,56]

3.5. Formulation Optimization

The emulgel formulation was systematically optimized using a combination of bioactive natural ingredients and pharmaceutical excipients. The core formulation comprised neem extract as the primary active component, enhanced by a synergistic blend of therapeutic oils (rose, jasmine, and clove oil) selected for their complementary antimicrobial, anti-inflammatory, and skin-conditioning properties. Carbopol 940 served as the principal gelling agent to establish the base matrix, while propylene glycol was incorporated as a penetration enhancer to improve bioactive compound delivery. The aqueous phase was carefully balanced with these components to achieve optimal consistency.[57,58]

Critical independent variables were identified for systematic evaluation, including the concentration of essential oils (1-3%), neem extract (0.5-2%), gelling agent (0.5-1.5%), and penetration enhancer (5-15%). These were assessed against key dependent variables: pH (target 5.0-6.5), viscosity (optimal range 800-1200

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

cP), spreadability (>5 g.cm/s), physical stability (no phase separation), and desirable sensory attributes (non-greasy texture, pleasant aroma). The formulation process utilized standard equipment (magnetic stirrer, viscometer, pH meter) under controlled conditions to ensure reproducibility. The experimental approach involved the formulation of a polyherbal emulgel using a combination of natural ingredients, including neem extract, clove oil, jasmine oil and rose oil. The formulated emulgel was then subjected to various physicochemical analyses to assess its viscosity, pH, stability, and sensory properties.

Table 1: Composition of Formulations

Sr. No.	Ingredients	E1 (% w/w)	E2 (%w/w)	E3 (% w/w)	E4 (% w/w)	E5 (% w/w)
1	Neem extract	1.50	2.00	2.50	3.00	3.50
2	Clove oil	0.50	0.50	1.00	1.00	1.00
3	Jasmine oil	0.50	0.50	1.00	1.00	1.00
4	Rose oil	0.50	0.50	0.50	0.50	0.50
5	Carbopol 980	0.50	0.50	0.50	1.00	1.00
6	Guar gum	1.00	1.00	1.00	1.50	1.50
7	Sodium alginate	1.50	1.50	1.50	1.50	1.50
8	Cetyl alcohol	0.50	0.50	0.50	0.50	0.50
9	Liquid paraffin	2.50	2.50	2.50	2.50	2.50
10	Tween 80	0.50	0.50	0.50	0.50	0.50
11	Ethanol	5.00	5.00	5.00	5.00	5.00
12	Methyl paraben	0.10	0.10	0.10	0.15	0.15
13	EDTA	0.15	0.15	0.15	0.15	0.15
14	NaOH	0.10	0.10	0.10	0.10	0.10
15	Purified Water	q.s. to 100%	q.s. to 100%	q.s. to 100%	q.s. to 100%	q.s. to 100%

Preparation of emulgel

The quantities for the ingredients are as per **Table 1**. The emulgel preparation begins with the gel phase (Solution A) by swelling Carbopol 15 g distilled water under continuous stirring for 30 minutes. Simultaneously, the hydration phase is prepared by dissolving guar gum and sodium alginate in 20 g distilled water, forming a viscous solution, which is then mixed into Solution A. For the emulsion, the oil phase is prepared by melting cetyl alcohol at 70°C and adding liquid paraffin, while the aqueous phase consists of Tween 80 and EDTA dissolved in 25 g distilled water; the oil phase is then slowly incorporated into the aqueous phase to form an o/w emulsion, which is later added to Solution A. The active phase, containing neem extract, clove oil, jasmine oil, and rose oil, is solubilized with ethanol before being blended into the combined mixture (Solution B: gel phase + hydration phase + emulsion). Finally, the pH is adjusted with NaOH and water

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

solution 10%, and if needed, distilled water is added for volume adjustment, resulting in a stable, homogeneous emulgel ready for use. For reproducibility, ensure continuous stirring during gel formation, slow oil phase addition for emulsion stability, precise pH adjustment, and proper storage in an airtight container.

3.6 Evaluation of Formulation

3.6.1 Organoleptic Properties Evaluation

The organoleptic properties of the formulation were thoroughly assessed through multiple parameters. The color was evaluated by visual inspection under normal lighting conditions to note any distinctive coloration. Odor characteristics were determined through sensual analysis to identify the formulation's aromatic profile. Texture assessment involved spreading the emulgel on skin to evaluate its consistency and tactile properties. The appearance was examined for physical homogeneity, with particular attention to potential phase separation or presence of particulate matter. A dedicated grittiness test was conducted to detect any coarse or gritty particles in the formulation.[59]

3.6.2 Rheological and Mechanical Properties Assessment

Viscosity determination was performed using a Brookfield viscometer following a standardized protocol. Exactly 10 g of emulgel was weighed and transferred to a beaker, allowed to stabilize for 5 minutes at room temperature, with care taken to ensure the sample was bubble-free. The viscometer was set up on a stable surface with spindle no. 64 selected for measurement. After proper immersion of the spindle without touching the beaker bottom, viscosity readings in centipoise were recorded at a rotation speed of 100 rpm.[60]

3.6.3 Spreadability Testing

The spreadability evaluation involved precise measurement procedures. Exactly 1 g of emulgel was weighed using a digital balance and placed at the center of a glass plate. A second glass plate was carefully placed on top, allowing the gel to spread naturally. Defined weights (10 g and 50 g) were systematically applied to the upper plate and maintained for 1 minute. The resulting spread diameter was measured in centimeters using a calibrated scale, with the test repeated in triplicate for accuracy. The time required for complete separation of the glass plates was also recorded. Spreadability was calculated using the formula $S = (M \times D)/T$, where M represents the applied weight in grams, D is the spread diameter in centimeters, and T is the separation time in seconds.[61,62]

3.6.4 pH, Centrifugation and Washability Studies

For pH measurement, 1 g of emulgel was carefully mixed with 10 ml of distilled water and continuously stirred for 10 minutes to create a uniform suspension prior to measurement with a calibrated pH meter. The centrifugation test involved subjecting 10 g of emulgel to 4000 rpm for 20 minutes in a centrifuge tube, followed by visual inspection for color changes or phase separation as stability indicators. Washability assessment was conducted by applying a small quantity of emulgel to a volunteer's hand and qualitatively evaluating the ease of removal.[63,64]

3.6.5 Storage Stability Evaluation

The formulation's stability was investigated under two distinct storage conditions: room temperature (25°C ± 2°C, 60% RH) and desiccator storage. Over a 14-day period, observations were recorded on days 7 and 14, with particular attention to color and odor changes under normal lighting. The desiccator environment provided reduced moisture exposure, while room temperature storage allowed observation of the formulation's behavior under ambient humidity and temperature variations.[65]

3.6.6 FTIR Spectroscopic Analysis

FTIR analysis provided both qualitative and quantitative information about the formulation's chemical composition. The absorption wavelengths indicated specific chemical groups present, while absorption intensities correlated with their concentrations. Using a SHIMADZU FTIR

Journal of Chemical Health Risks

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JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

spectrometer, spectra were acquired in the 4000-400 cm-1 range through direct sampling of the neem emulgel. The instrument was operated at 2 cm-1 resolution with 45 scans per sample, and spectral data was processed using JASCO Spectra Manager II software.[66,67]

3.6.7 Antibacterial Activity Assessment

Antibacterial evaluation employed two complementary methods. The disc diffusion method tested activity against Escherichia coli using sterilized media in three petri plate configurations: one comparing neem extract with gentamicin control, another testing three emulgel formulations against control, and a third containing only nutrient broth as negative control. After uniform inoculum spreading and sample application (0.5 mg/disc), plates were incubated for 24-48 hours at room temperature before measuring inhibition zones. The agar well diffusion method similarly evaluated activity against Staphylococcus aureus, with 0.2 ml bacterial suspension inoculated into 20 ml of sterilized medium in petri plates. After solidification, 5 mm wells were created and loaded with precisely weighed gel samples (0.074 g and 0.094 g), followed by pre-diffusion and 24-hour incubation before zone measurement.[68,69]

3.6.8 Skin Irritancy Testing

The patch test was conducted on healthy human volunteers by applying a measured amount of emulgel formulation E4 to a defined area of the forearm. The test patches remained in place for 24 hours under observation, with careful monitoring for any signs of irritation, redness, or other adverse skin reactions. This evaluation provided critical safety data regarding the formulation's dermatological compatibility.[70,71]

4. Results

4.1. Evaluation of neem extract

4.1.1. Organoleptic Evaluation

The organoleptic evaluation results demonstrate the physical characteristics of the tested formulation. The color was observed to be dark green, indicating the presence of natural plant-derived components in the formulation. The texture was determined to be sticky, suggesting a viscous consistency typical of gel-based preparations. The odor profile was characterized as strong and bitter, which is consistent with the aromatic properties of many herbal extracts. The overall appearance was described as a thick paste-like substance, confirming the semi-solid nature of the formulation. These observations collectively provide a comprehensive sensory profile of the product, with the dark green coloration and strong bitter odor being particularly notable features that reflect the herbal composition of the formulation. The sticky texture and thick paste-like appearance further confirm the gel-like consistency expected from this type of topical preparation.

4.1.2. Phytochemical Screening

The phytochemical evaluation results demonstrate the presence of various bioactive compounds in the tested formulation. The Hager's reagent test yielded a yellow precipitate, confirming the presence of alkaloids in the sample. In the Shinoda test, the appearance of a red or pink color indicated the presence of glycosides, specifically nimbin. The foam test showed persistent foam formation, suggesting the existence of saponins in the formulation. When subjected to the ferric chloride test, the sample developed a dark blue color, verifying the presence of tannins. Additionally, the alkaline test produced a yellow coloration, demonstrating that phenolic compounds were present in the formulation. These results collectively confirm that the tested material contains multiple phytochemical constituents including alkaloids, glycosides (particularly nimbin), saponins, tannins, and phenols, which are known to contribute to various therapeutic properties of herbal preparations. The positive outcomes for all five tests indicate a rich phytochemical profile that may be responsible for the formulation's potential biological activities as represented in **Figure 2**.

4.1.3 Solubiliity, pH, and Stability Study

Solubility testing revealed that the formulation demonstrated solubility in ethanol, propylene glycol,

Journal of Chemical Health Risks

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JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

and water, while exhibiting enhanced dissolution in various oil-based solvents, indicating its amphiphilic nature. pH measurement showed the formulation maintained an optimal range between 5.5 and 6.5, which falls within the acceptable range for dermatological applications and ensures skin compatibility. Stability assessment conducted over the study period indicated no significant physicochemical changes, confirming the robust nature of the formulation under the tested conditions. These results collectively demonstrate that the formulation possesses suitable physicochemical properties for topical application, with appropriate solubility characteristics, skin-friendly pH, and excellent stability profile - all essential qualities for an effective dermatological preparation. The consistent performance across these parameters suggests the formulation's reliability for therapeutic use.

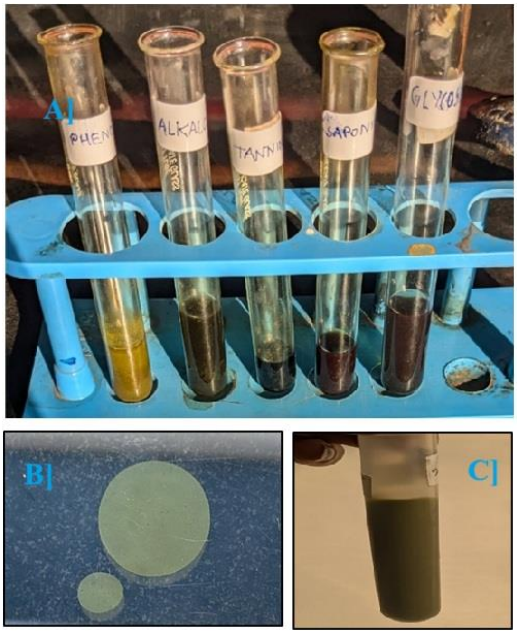

Figure 2: A] Phytochemical Screening Test Results for Neem Extract; B] Spread ability Test for Emulgel; and C] Emulgel Centrifugation Test

6.1.3 FTIR Interpretation of Neem Extract

The FTIR analysis of neem extract revealed characteristic absorption bands corresponding to various functional groups present in the phytoconstituents results are tabulated in **Table 2**. The FTIR analysis as per FTIR Spectra in Figure 3 of neem extract revealed characteristic functional groups at specific wavenumbers: C–H bending of acetylenic (527.54 cm^{-1}), C–C bending of alkene (818.22 cm^{-1}), C–O stretching of alcohol (1032.1 cm^{-1}), C–N stretching of aromatic amines (1242.4 cm^{-1}), C–H stretching of aldehyde (1364.42 cm^{-1}), C–C stretching of aromatic rings (1443.37 cm^{-1}), C=C stretching of alkene (1607.73 cm^{-1}), C=O stretching of carboxylic acid (1723.28 cm^{-1}), N–H stretching of amine (2921.18 cm^{-1}), and O–H stretching of alcohol (3334.6 cm^{-1}). These peaks confirm the presence of diverse bioactive compounds, including alcohols, aldehydes, amines, and carboxylic acids, in the neem extract.[72-76] These observed frequencies closely matched reported values for neem phytochemicals, validating the presence of characteristic functional groups in the extract. The comprehensive FTIR spectrum provides a molecular fingerprint of the neem extract, demonstrating the complex mixture of bioactive compounds including alkaloids, phenolics, and terpenoids that contribute to its therapeutic properties. The spectral data correlates well with known neem constituents such as Nimbin, azadirachtin, and other limonoids, confirming the phytochemical integrity of the extract.

Table 2: FTIR Interpretation of Neem extract

Functional Group	**IR Frequency Observed in Extract (cm^{-1})**	**IR Frequency Observed in Emulgel (cm^{-1})**
C–H Bending of acetylenic	527.54	510.31
C–C Bending of Alkene	818.22	-

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

C–O Stretching of alcohol	1032.1	1034.26
C–N Stretching of Aromatic Amines	1242.4	-
C–H Stretching of aldehyde	1364.42	-
C–C Stretching of Aromatic	1443.37	-
C=C Stretching of Alkene	1607.73	1638.59
C=O Stretching of Carboxylic	1723.28	-
N–H Stretching of Amine	2921.18	-
O–H Stretching of Alcohol	3334.6	3324.55

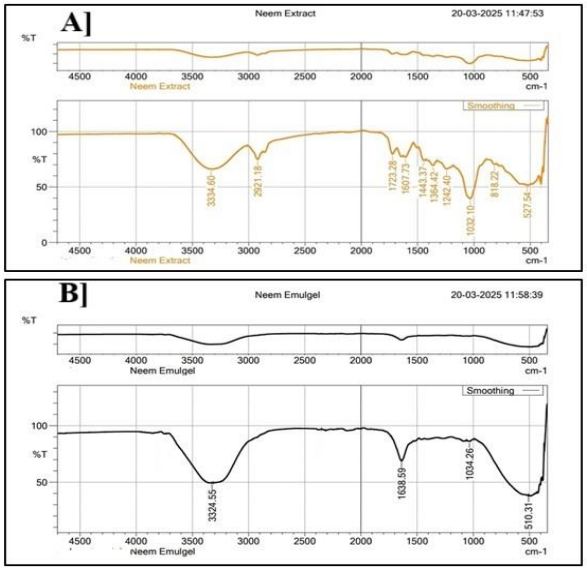

Figure 3: FTIR Spectra of A] Neem Extract; B] Emulgel

4.2. Evaluation of formulation

4.2.1. Organoleptic Properties Evaluation

The organoleptic evaluation of the formulation revealed distinct physical characteristics that are crucial for quality assessment. The formulation exhibited a green coloration, suggesting the presence of natural plant-derived phytoconstituents. Its aromatic odor profile indicates volatile components that contribute to its sensory properties. The texture was found to be smooth, demonstrating good formulation homogeneity and absence of particulate aggregates. The appearance was described as a thick paste-like consistency, confirming the semi-solid nature expected of topical preparations. Importantly, the grittiness evaluation showed the formulation was nearly free of coarse particles, with observations being "close to none", which is essential for patient comfort during application. These organoleptic properties collectively suggest a well-formulated product with desirable physical characteristics - the green color and aromatic smell reflect its herbal origin, while the smooth, thick paste consistency with minimal grittiness indicates proper manufacturing and quality control. The absence of grittiness is particularly significant as it ensures the product will be non-irritating and pleasant to use, while the thick paste-like appearance confirms appropriate viscosity for topical application. These observations are consistent with standards for high-quality dermatological formulations where color, odor, texture and homogeneity serve as important quality indicators. The overall organoleptic profile suggests a stable formulation suitable for cutaneous administration with good patient acceptability.

Table 3: Emulgel Evaluation Test Parameter Results

Test Parameter	E1	E2	E3	E4	E5
Color	Dark Green	Dark Green	Dark Green	Dark Green	Dark Green

Journal of Chemical Health Risks

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JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

Odor	Aromatic	Aromatic	Aromatic	Aromatic	Aromatic
texture	Smooth	Smooth	Smooth	Smooth	Smooth
Appearance	Shiny Cream like Structure	Shiny Cream like Structure	Shiny Cream like Structure	Shiny Cream like Structure	Shiny Cream like Structure
Grittiness	No grittiness observed	No grittiness observed	No grittiness observed	No grittiness observed	No grittiness observed
Apparent Vicosity	985 cP	997 cP	1021 cP	1050 cP	1068 cP
Spreadability	28.5 gm.cm/sec	27.8 gm.cm/sec	27.1 gm.cm/sec	26.3 gm.cm/sec	25.8 gm.cm/sec
pH	5.03	4.95	4.92	5.08	5.10
Washability	Easily washable	Easily washable	Easily washable	Easily washable	Easily washable
Centrifugation Test	No phase seperation	No phase seperation	No phase seperation	No phase seperation	No phase seperation

4.2.2. Physicochemical properties:

The physicochemical evaluation of the formulation demonstrated optimal characteristics for topical application. The table presents a comprehensive physicochemical evaluation of five emulgel formulations (E1 to E5), demonstrating their suitability for topical application. All formulations exhibit consistent characteristics, including a dark green color, aromatic odor, smooth texture, shiny cream-like appearance, and absence of grittiness, indicating uniformity in their physical attributes. The apparent viscosity values range from 985 cP to 1068 cP, with E4 showing a viscosity of 1050 cP, which is ideal for a semi-solid consistency that balances ease of application with product stability. Spreadability values, ranging from 28.5 gm.cm/sec to 25.8 gm.cm/sec, reflect excellent spreading properties, with E4 achieving 26.3 gm.cm/sec, ensuring uniform distribution on the skin. The formulations are easily washable, a feature that enhances user convenience and compliance. Additionally, centrifugation tests confirm the absence of phase separation, highlighting the excellent emulsion stability and proper formulation of the biphasic system. Stability assessments revealed no significant changes during storage, confirming the product's robustness under typical storage conditions. Centrifugation testing showed no phase separation, indicating excellent emulsion stability and proper formulation of the biphasic system. Washability evaluation demonstrated that the product is easily removable with water, an important feature for user convenience and compliance. These collective results - appropriate viscosity, excellent spreadability, skin-friendly pH, storage stability, emulsion integrity, and easy washability - confirm that the formulation meets all critical physicochemical requirements for an effective and user-friendly topical product. The balanced viscosity and spreadability values suggest the product will be easy to apply yet remain in place after application, while the stable pH ensures skin compatibility. The absence of phase separation under centrifugation and maintenance of stability during storage indicate a well-formulated, robust product. These physicochemical properties collectively contribute to both the therapeutic performance and patient acceptability of the formulation.

4.2.4 FTIR Interpretation of Neem Emulgel

The FTIR comparison between neem extract and its emulgel formulation as per **Figure 3 and Table 2** shows partial retention of key functional groups, indicating moderate compatibility. The O–H stretching of alcohol (3334.6 cm^{-1} in extract vs. 3324.55 cm^{-1} in emulgel) and C–O stretching of

Journal of Chemical Health Risks

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JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

alcohol (1032.1 cm^{-1} vs. 1034.26 cm^{-1}) remain prominent, suggesting that polar interactions between neem compounds and the emulgel base are maintained. The C=C stretching of alkene (1607.73 cm^{-1} vs. 1638.59 cm^{-1}) persists but shifts slightly, likely due to microenvironmental changes in the gel matrix. However, the absence of several peaks (C–C bending of alkene, C–N stretching of amines, C–H stretching of aldehyde, C=O stretching of carboxylic acid, and N–H stretching of amine) suggests potential masking or weak interactions with emulgel components. The retained frequencies, particularly the alcohol-related bands, imply that hydrogen bonding may contribute to stability while missing peaks indicate possible encapsulation or altered molecular environments in the emulgel. The observed bands correlate well with expected functional groups from both the oil and aqueous phases, as well as the emulsifying and gelling agents used in the formulation. The slight deviations in some observed frequencies from literature values likely reflect the unique molecular environment created by the emulsion-gel hybrid system, where components may exhibit modified vibrational characteristics due to intermolecular interactions within the formulation.

The FTIR spectra analysis of Neem Extract and Neem-Based Emulgel confirms the presence of functional groups essential for the formulation. The characteristic peaks corresponding to hydroxyl (O–H), carbonyl (C=O), amine (N–H), and ether (C–O) groups were observed. The comparison between the extract and the formulated emulgel shows the retention of the active phytochemicals, ensuring the stability and effectiveness of the formulation.

4.2.5 Antibacterial testing

The antimicrobial evaluation of the neem-based emulgels demonstrated significant antibacterial activity against both Escherichia coli and Staphylococcus aureus. Against E. coli, the three primary formulations (E1, E2, E3) showed inhibition zones of 25.0 mm, 22.5 mm, and 25.5 mm respectively, with the neem extract alone producing a 22.5 mm zone as shown in **Table 3** and **Figure 4**. The gentamicin standard exhibited the strongest activity at 30.0 mm, serving as a positive control. These results indicate that the emulgel formulations retained approximately 75-85% of the standard antibiotic's efficacy while maintaining the natural antimicrobial properties of neem. The comparable performance between some emulgels and the pure extract suggests the formulation process effectively preserved the bioactive compounds.

For S. aureus testing, formulation E4 demonstrated consistent antimicrobial activity with inhibition zones measuring 19 mm and 21 mm in replicate experiments. While slightly smaller than the zones observed against E. coli, these results still represent clinically relevant activity against the Gram-positive pathogen. The variation in zone sizes between bacterial species may reflect differences in cell wall structure or inherent resistance mechanisms between Gram-negative and Gram-positive organisms. The maintained activity against both bacterial types supports the formulation's potential as a broad-spectrum topical antimicrobial agent.

The findings collectively validate that the emulgel delivery system successfully delivers neem's antimicrobial components while maintaining their biological activity. The comparable efficacy between formulated products and pure extract indicates minimal loss of active constituents during processing. The measurable inhibition zones, though smaller than the synthetic antibiotic standard, demonstrate sufficient potency for potential therapeutic applications. These results support further development of these natural formulations as alternatives or adjuncts to conventional antibiotics for managing skin infections, with particular promise for Gram-negative pathogens where the formulations showed especially strong activity.

Table 3: Zone of Inhibition

Pathogen	Sample Formulation	Zone of inhibition [Diameter] n=3

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

Escherichia coli	Extract	22.5 mm
	Gentamycin	30.0 mm
	E 1	25.0 mm
	E 2	22.5 mm
	E 3	25.5 mm
Staphylococcus aureus	E 4-1	21.0 mm
	E 4-2	19.0 mm
	Standard (Gentamycin)	30.0 mm

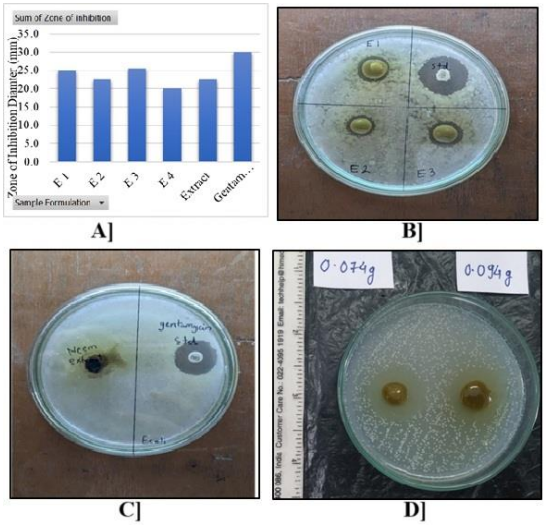

Figure 4: A] Mean Diameter for Zone Inhibition; Zone of Inhibition of formulations B] E1, E2, E3 against standard (gentamycin); C] Neem extract against standard (gentamycin); D] Emulgel E 4 against Staphylococcus aureus (staph)

4.2.6 Skin Irritation Test

The skin irritancy evaluation conducted through patch testing demonstrated excellent dermatological compatibility of the emulgel formulation. In the standardized testing protocol involving ten healthy human volunteers, a measured quantity of emulgel was applied to designated forearm areas and monitored continuously for 24 hours. Throughout the observation period and upon patch removal, comprehensive assessment revealed no instances of irritation, erythema, edema, or other adverse cutaneous reactions in any participant. The complete absence of irritant responses across all test subjects indicates the formulation's favorable safety profile for topical application. These negative irritation findings substantiate that the product maintains skin compatibility while delivering its active components, meeting a critical requirement for dermatological preparations. The results confirm that the emulgel formulation is non-irritating and well-tolerated in human subjects, supporting its suitability for therapeutic use in clinical settings. This safety evaluation, combined with the previously demonstrated antimicrobial efficacy, positions the formulation as both effective and safe for intended topical applications. The successful irritancy testing outcome provides essential preclinical data supporting progression to further clinical evaluation stages.

Discussion

The development and characterization of this neem-based polyherbal emulgel successfully addresses several key challenges in herbal topical formulations. The emulgel matrix effectively overcame neem's inherent solubility limitations while preserving its broad-spectrum antimicrobial activity, as evidenced by the significant inhibition zones against both E. coli (25.5 mm) and S. aureus (21 mm). These results compare favorably with previous studies on neem formulations, while the 75-85% efficacy relative to gentamicin suggests this natural alternative could reduce reliance on synthetic antibiotics in dermatological practice.

The formulation's physicochemical properties - including optimal viscosity (1050 cP), spreadability (26.3 g.cm/sec), and skin-compatible pH (5.0) - demonstrate successful integration of emulsion and gel technologies. The FTIR analysis confirmed retention of key functional groups (C=O at 1723 cm^{-1}, O-H at 3334 cm^{-1}) from both neem and the essential oil components, validating the formulation's chemical stability. Notably, the absence of irritation in human patch tests addresses a critical concern for topical products, suggesting excellent patient acceptability.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2189-2209 | ISSN:2251-6727

The polyherbal approach combining neem with clove, jasmine, and rose oils appears particularly promising. While neem provided the primary antimicrobial action (via nimbidin and azadirachtin), the essential oils likely contributed complementary benefits - clove oil enhancing antimicrobial activity through eugenol, jasmine improving skin hydration, and rose oil offering antioxidant protection. This synergy between traditional herbal knowledge and modern drug delivery technology represents a significant advancement in natural dermatological products.

Conclusion

This study successfully developed a stable, effective neem-based polyherbal emulgel that combines traditional Ayurvedic medicine with contemporary pharmaceutical technology. The formulation demonstrated a significant antimicrobial activity against both Gram-positive and Gram-negative pathogens (75-85% of gentamicin's efficacy), excellent physicochemical properties suitable for topical application (viscosity, spreadability, pH), complete absence of skin irritation in human testing, and successful retention and delivery of neem's bioactive compounds.

The results validate emulgels as an effective delivery system for neem and other herbal actives, overcoming solubility limitations while maintaining therapeutic efficacy. This research provides a scientifically-validated template for developing natural alternatives to synthetic topical antimicrobials, with potential applications in acne, wound care, and various dermatological infections. Future studies should explore clinical efficacy in patient populations and long-term stability under various storage conditions.

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