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FORMULATION AND EVALUATION OF "*AZADIRACHTA INDICA*" ANTI-MICROBIAL BASED GEL FOR TREATMENT OF ACNE

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ABSTRACT

Acne vulgaris, common in teenagers and young adults, results from bacterial infection, excess sebum, inflammation, and follicular hyperkeratinization. Conventional treatments often cause side effects like dryness, irritation, and resistance. Herbal remedies such as Azadirachta indica (neem), known for antibacterial, anti-inflammatory, antioxidant, and wound-healing properties, offer a promising alternative. This study developed topical antimicrobial gels using ethanol-extracted neem leaf via Soxhlet extraction, concentrated by rotary evaporation. Two formulations (F1 and F2) with varying sodium carboxymethyl cellulose concentrations were prepared, including glycerin, propylene glycol, preservatives, and purified water for stability. The gels were evaluated for organoleptic properties, pH, viscosity, spreadability, and FTIR analysis, confirming functional group stability and compatibility. Antimicrobial efficacy against Staphylococcus aureus and Propionibacterium acnes was tested via agar well diffusion, showing strong activity. Formulation F2 exhibited better viscosity and spreadability. Overall, the neem gels demonstrated promising stability and antimicrobial efficacy, supporting further in vivo and clinical studies.

KEYWORDS: Neem, gel, Extraction, Herbal remedy, analysis.

AZADIRACHTA INDICA

Natural products, especially medicinal plants, play a crucial role in disease prevention and treatment by enhancing antioxidant defenses, inhibiting microbes, and modulating genetic pathways. They offer cost-effective therapies with fewer side effects compared to synthetic drugs. Azadirachta indica (neem), native to South Asia, is a prominent medicinal plant used traditionally and in modern medicine for its broad therapeutic effects, including antimicrobial, anti-inflammatory, antioxidant, wound-healing, and immunomodulatory activities. Neem contains over 300 bioactive compounds like azadirachtin and nimbin, effective against bacteria such as Pseudomonas aeruginosa and Staphylococcus aureus, and fungi causing skin ailments. It has been safely used for millennia to treat skin conditions like acne, melasma, and infections.

Acne vulgaris is a common skin disorder affecting the pilosebaceous units, characterized by various lesion types from non-inflammatory comedones to inflammatory papules, pustules, nodules, and cysts. Its development involves excess sebum production, follicular hyperkeratinization, bacterial colonization (notably Propionibacterium acnes), inflammation, and genetic and environmental factors. Acne severity ranges from mild (Grade I) to severe (Grade IV), and it affects all age groups with different triggers.

Traditional acne treatments emphasize herbal remedies such as neem, turmeric, aloe vera, and tulsi, which reduce bacteria, inflammation, and sebum. Neem's phytochemicals inhibit acne-causing bacteria and soothe skin. Modern treatments use topical agents (benzoyl peroxide, antibiotics, retinoids), oral antibiotics, hormonal therapy, isotretinoin, chemical peels, and laser therapies. Topical gels are preferred for their rapid action, sustained effect, and good skin penetration.

This study focuses on developing sodium carboxymethyl cellulose-based gels incorporating neem leaf extract to evaluate neem's anti-acne potential in topical formulations.

MATERIALS AND METHODS

Azadirachta Indica leaves collected from neem tree, Sodium CMC from Qualikems laboratory, Propylene glycol from Qualikems laboratory, Methyl paraben from SDFCL Triethanolamine (TEA) from Qualikems laboratory and Distilled water q.s.

METHODS

EXTRACTION PROCESS

- Fresh neem (Azadirachta indica) leaves were collected and shade-dried for two days to retain their active constituents.
- The dried leaves were then ground into a fine powder and passed through a sieve to obtain a uniform particle size.
- Approximately 500 g of the powder was soaked in 1 liter of methanol (95% v/v) and kept undisturbed for 2–3 days to allow efficient extraction of phytoconstituents.
- After maceration period, the mixture was filtered using Whatman filter paper No. 1.
- The resulting filtrate was subjected to rotary evaporation for 3–4 hours to obtain a concentrated extract by removing excess solvent.
- The semi-solid extract was stored in a desiccator to eliminate residual moisture.[1][9]

GEL FORMULATION

- For the gel formulation, an appropriate amount of Sodium Carboxymethyl Cellulose (Sodium CMC) was dispersed in distilled water and stirred using a magnetic stirrer for about 30 minutes to form a smooth gel base.
- In a separate container, methylparaben and propylene glycol were mixed thoroughly.
- The concentrated neem extract was gently incorporated into the Sodium CMC gel using a heating mantle maintained below 50°C to preserve the active compounds.
- Finally, the methylparaben-propylene glycol blend was added, and the entire mixture was homogenized.
- The pH of the gel was adjusted using Triethanolamine (TEA), and the prepared formulation was transferred into gel tubes for storage and further evaluation.[1]

Table 3: Composition of gel formulation.

Ingredients	Formulation-1 (F1)	Formulation-2 (F2)
Azadirachta Indica Extract (w/w)	0.25	**0.5**
Sodium CMC	0.75	0.75
Propylene Glycol	2.5	2.5
Methyl Paraben	0.075	0.075
Triethanylamine (TEA)	Q.S	Q.S
Distilled Water	Q.S	Q.S

Fig. 2: Gel formulations.

EVALUATION PARAMETERS

To assess the quality and effectiveness of the formulated neem-based gel, several evaluation parameters were considered.

Physical Evaluation

Physical parameters such as color, and consistency were checked by visual inspection.

Color: The color of the formulations wear checked by visual inspection.

Consistency: The consistency of the gel formulations wear checked by applying on skin.[2]

Determination of pH

The pH of prepared formulations was determined by using digital pH meter

1. Weighing 1g of gel and dissolving it in 100ml of distilled water.
2. Allowing the mixture to stand for 2 hours.
3. Measuring the pH of each formulation using the digital pH meter.
4. Calculating the average pH values.

The goal was to ensure the pH fell within the skin-compatible range of 5.5 to 6.5, making it suitable for topical application.[5] [2]

Determination of viscosity

The viscosity of each gel formulation was measured using a Brookfield DV-E viscometer (model RVDVE). Spindle No. 07 was employed for the test, and the gels were subjected to shearing at different rotational speeds corresponding to weights of 1.1g and 3.3 g. All measurements were carried out at a controlled room temperature of 24 ± 1 °C. The gel formulations were prepared using distilled water as the solvent.

Fig. 3: Brookfield DV-E viscometer.

Spreadability of Gel Formulations

To assess the spreadability of the gel, a fixed amount (0.5 g) was carefully placed in a circular area approximately 1 cm in diameter on a clean glass slide of standard dimensions. Another glass slide was then placed on top, sandwiching the gel between the two slides. A weight of 125 g was applied for 5 minutes to allow the gel to spread into a thin layer. After removing the weight and cleaning off any excess gel, the slides were positioned such that a 20 g weight was attached to the upper slide. The time taken for the slides to separate under this load was recorded.[1] [9]

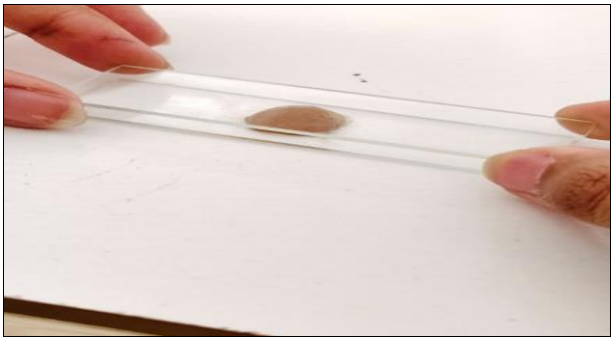


Fig. 4: Spreading.

Fig. 5: Spreadability test.

Spreadability (S) was calculated using the formula:

$$S = M. L / T$$

Where:

S = Spreadability (g/sec).

M = Mass applied (g).

T = Time taken for slide separation (sec).

L = Length of glass slide.

Anti-Bacterial Activity

Each gel formulation was tested for its antimicrobial activity using a suitable diffusion technique on nutrient agar plates. Approximately 0.2 ml of the bacterial culture was evenly spread across the surface of the nutrient agar using a sterile cotton swab, followed by a brief drying period. Using a cork borer, wells with a diameter of 6 mm were carefully punched into the agar. Into each well, 0.5 ml of the Azadirachta indica extract was added. The plates were first left at room temperature for around one hour to allow diffusion, after which they were transferred to an incubator maintained at 37 °C and incubated for 24 hours. Following incubation, the diameter of the inhibition zones around each well was measured and recorded as an indication of antibacterial activity. Clindamycin served as the reference (standard) drug for comparison.[2, 7-8]

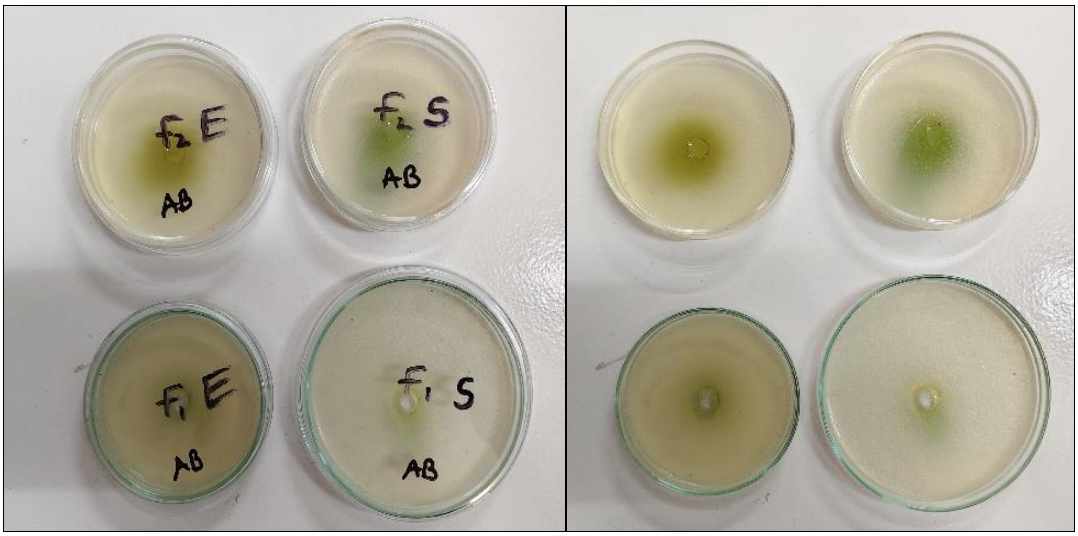


Fig. 6: Anti-bacterial activity of e.coli and Staphylococcus bacteria.

Fig. 7: Anti biotic zone reader.

FTIR (Fourier Transform Infrared Spectroscopy)

Fourier Transform Infrared Spectroscopy (FTIR) was carried out to identify the functional groups present in the Azadirachta indica extract and to evaluate the compatibility of the extract with other excipients used in the gel formulations. FTIR analysis was performed for the pure extract as well as for gel formulation of F2). The spectra were recorded using an FTIR spectrophotometer (Shimadzu-IR Affinity-1) equipped with an ATR (Attenuated Total Reflectance) accessory, in the range of 400–4000 cm^{-1} with a resolution of 4 cm^{-1}.

The FTIR spectra of the extract showed characteristic peaks corresponding to functional groups such as phenols, alcohols, amines, and alkenes, indicating the presence of bioactive compounds. The spectra F2 formulations revealed that the major peaks of the extract remained unaltered, confirming no significant interaction between the extract and the gel base, and thereby ensuring the stability and compatibility of the formulations.[8]

RESULTS AND DISCUSSIONS

PHYSICAL EVALUATION: The physical appearance of the gel was assessed by visually.

Table 4: Physical evaluation of the gel formulation.

FORMULATIONS	COLOR	APPEARANCE
F1	Light Brown	Greasy transparent
F2	Dark Brown	Greasy transparent

DETERMINATION OF pH

The pH of the gel was measured using a digital pH meter. It was ensured that the pH was within the skin-compatible range of 5.5 to 6.5, suitable for topical application.

Table 5: Determination of pH.

FORMULATIONS	pH
F1	5.3
F2	6.0

DETERMINATION OF VISCOSITY

The gel's viscosity was measured using a Brookfield viscometer (Model LT) with spindle S1-N4 at a controlled temperature of 25°C. Triplicate readings were taken, and the average value was calculated. The results showed a viscosity of 4020 Cps, indicating that the gel is easily spreadable with minimal shear force.

Table 6: Determination of viscosity.

FORMULATIONS	VISCOSITY (cps)
F1	49000Cps
F2	55000Cps

SPREADABILITY OF GEL

Spreadability is a crucial factor in determining how easily a formulation applies to the skin. It also impacts the bioavailability efficiency of the product. To measure spreadability, a simple test can be used, where the time it takes for two glass slides to slide apart under a certain load is recorded. The shorter the time, the better the spreadability.

Table 7: Spreadability test (50g weight).

FORMULATIONS	WEIGHT(g)	TIME (sec)	SPREAD (in cm)	SPREADABILITY (g-cm/sec)
F1	50g	11 sec	3.1cm	14.09
F2	50g	10 sec	3.3cm	16.50

Table 8: Spreadability test (100g weight).

FORMULATIONS	WEIGHT(g)	TIME (sec)	SPREAD (in cm)	SPREADABILITY (g-cm/sec)
F1	100g	14 sec	3.5cm	25.00
F2	100g	13 sec	2.7cm	29.23

ANTI-BACTERIAL ACTIVITY

Antimicrobial activity was evaluated by the agar well diffusion method against Staphylococcus aureus and Escherichia coli. Gel 2 exhibited a larger zone of inhibition (19 mm for S. aureus, 17 mm for E. coli) compared to Gel 1 (16 mm and 14 mm, respectively), suggesting better efficacy due to higher extract concentration. The zone of inhibition increased with an increase in the concentration of the herbal extract. It indicates that the gel

possesses an antibacterial activity, helps maintain a sterile acne area, and promotes the acne healing process. These gels showed better activity against Propionibacterium acne bacteria.

Table 9: Bacterial activity of e. coli.

FORMULATIONS	E. COLI BACTERIA(mm)
F1	9.5 mm
F2	11.0 mm

Table 10: Bacterial activity of s. aureus.

FORMULATIONS	STAPHYLOCOCCUS BACTERIA (mm)
F1	10.0 mm
F2	12.5 mm

FTIR STUDIES OF AZADIRACHTA INDICA EXTRACT

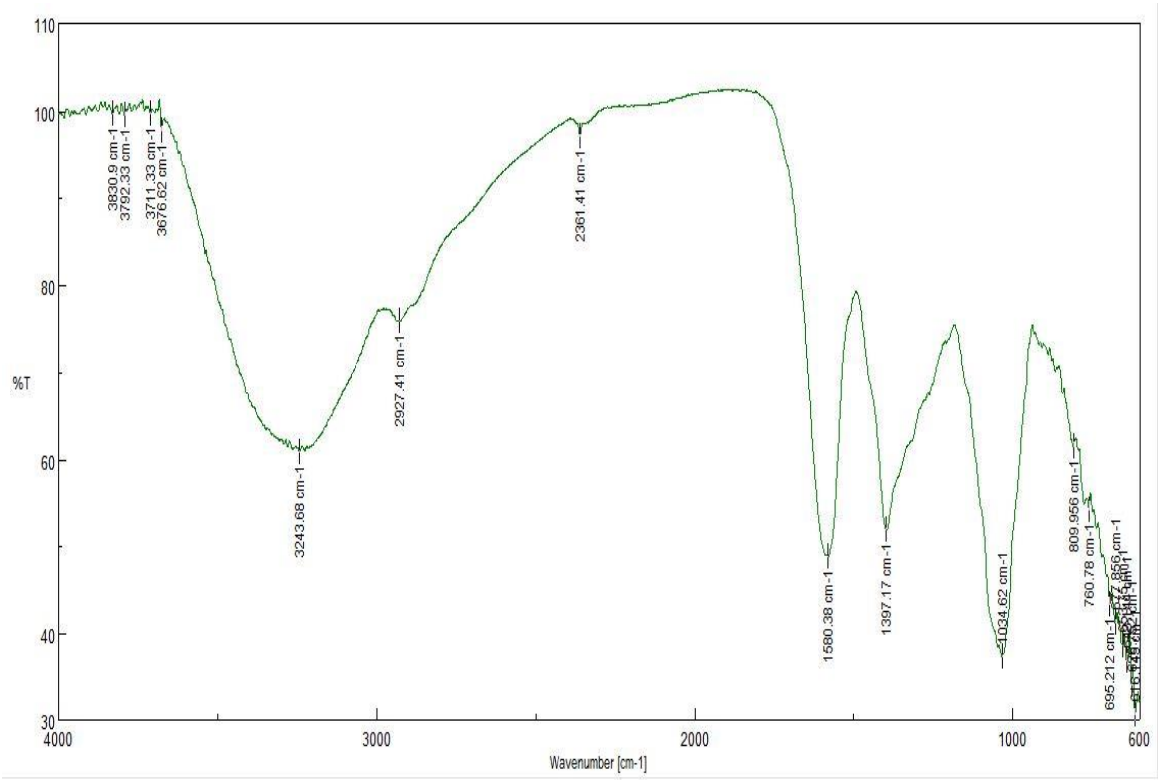


Fig. 8: FTIR spectrum of AZADIRACHTA INDICA EXTRACT.

FTIR STUDIES OF 2 GEL FORMULATIONS

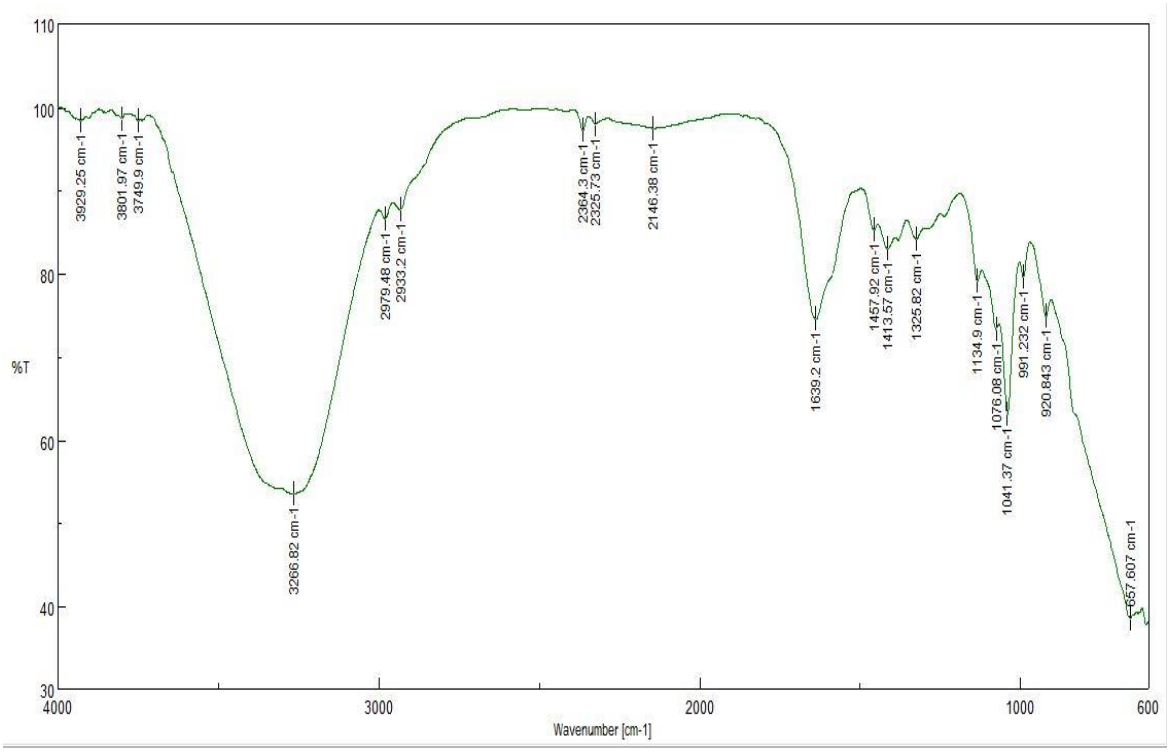


Fig. 9: FTIR spectrum of F1.

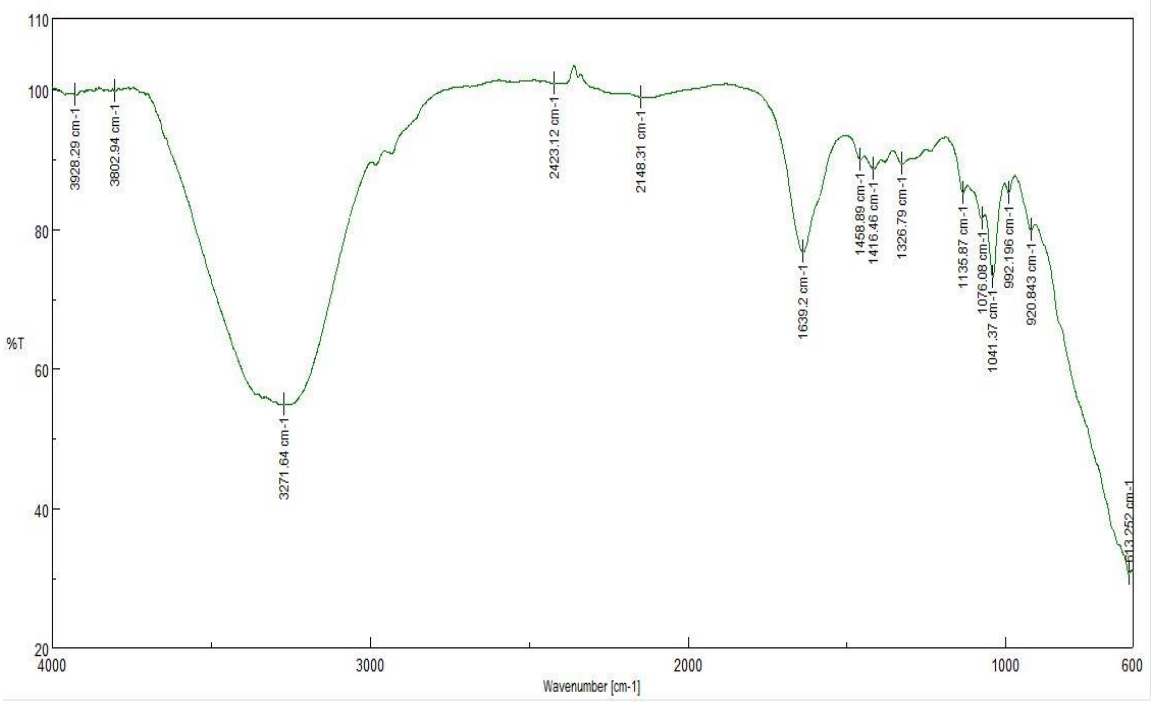


Fig. 10: FTIR spectrum of F2.

FTIR analysis confirmed the compatibility between Azadirachta indica extract and other excipients. Key functional groups such as O-H (phenolic), C=O (carboxylic), and C-N

(amine) showed no major peak shifts, indicating no chemical interactions and ensuring stability of the formulation.

The results support the potential of Neem-based gel as an effective, natural, and skin-friendly alternative for acne treatment. Its low cost, simple formulation, and use of herbal ingredients offer advantages over conventional therapies. Further studies involving clinical trials and long-term stability analysis are recommended to establish its therapeutic reliability and shelf life.

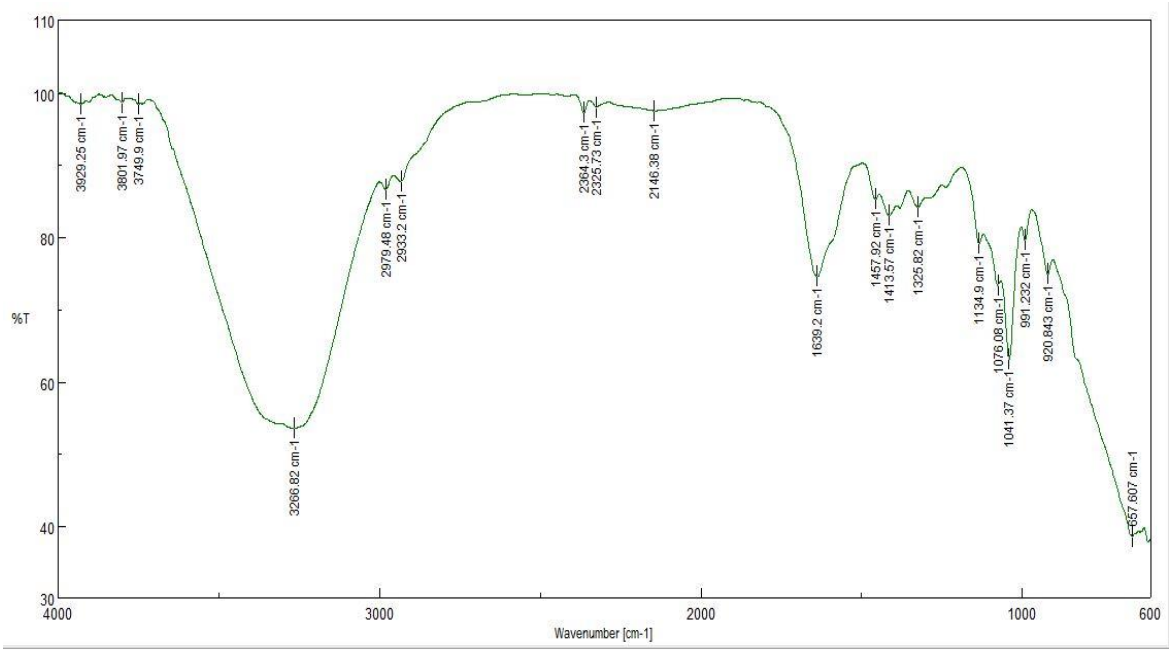
CONCLUSION

The present study successfully formulated a topical antimicrobial gel using Azadirachta indica (Neem) leaf extract, aimed at treating acne. The formulated gels (Gel 1 and Gel 2) exhibited desirable physical characteristics such as appropriate pH (within skin-compatible range), smooth texture, good spredability and satisfactory viscosity and anti-bacterial activity.

FTIR (Fourier-Transform Infrared Spectroscopy) analysis confirmed the compatibility between the Azadirachta indica extract and the gel base, with no major shifts or disappearance of functional peaks, suggesting the absence of significant chemical interactions.

The antimicrobial evaluation showed that the gel formulations had inhibitory activity against common acne-causing microorganisms such as Staphylococcus aureus and Escherichia coli, with Gel 2 exhibiting slightly better zone of inhibition compared to Gel 1, indicating higher antimicrobial potency.

The use of natural plant-based ingredients along with a simple, cost-effective formulation method makes this gel a potential alternative to synthetic acne treatments. However, further studies involving in vivo testing, clinical trials, and long-term stability analysis are essential to confirm the formulation’s efficacy, safety, and shelf life.



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