

A Novel Phytopharmaceutical Gel Incorporating Azadirachta indica Extract for Enhanced Anti-Acne Efficacy: Formulation and Characterization

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ABSTRACT:

The objective of this study was to produce a carbopol940 based gel formula containing an Azadirachta indica leaf extract and evaluate its anti-acne potential. Acne is one of the most prevalent skin ailments affecting almost all teenagers or that affects virtually all individual at least once during life. The modern measures regarding the treatment of acne are more or less failure further it has some limitations cost effective & some side effect To overcome from all these a good herbal approach should be reached.

The ethanolic extract was derived from the dried leaves of Azadirachta indica was subjected to a phytochemical evaluation. Three gel formulations of carbopol 940 containing an Azadirachta indica extract in three different concentrations, i.e., 1, 2, and 3% w/w were prepared. These gels were evaluated for their physical appearance, antimicrobial activity, skin irritability, pH, spreadability, and viscosity. The prepared formulas were stable, greenish and homogeneous. None of them showed irritation to the skin. Gel-3 exhibited the highest antimicrobial potential against Propionibacterium acne, the main causative organism of acne with a zone of inhibition of 16.2_±0.6 mm.

KEYWORDS: Azadirachta indica, Gel, Anti- acne

INTRODUCTION:

The plant product or natural products show an important role in disease prevention and Treatment through the enhancement of antioxidant activity, inhibition of bacterial growth, and modulation of genetic pathways. Azadirachta indica (family: Meliaceae) is a medicinal plant, commonly known as neem, found in India, Pakistan, Bangladesh, and Nepal, and is widely used to treat various diseases. Neem has been commonly used in Ayurveda, Unani, Homoeopathic, and Siddha medicine and has become prominent in modern medicine. The limonoids and azadirachtin found in neem seeds have insecticidal effects, but are safe for human beings. The leaf extract, seed oil, and bark of the neem are medicinally used in folk medicine for Constipation, respiratory disorders, leprosy, and intestinal helminthiasis and they promote good health. Neem also possesses antipyretic, anti-inflammatory, antimycotic, antimicrobial, immunomodulatory, cardiovascular, antihyperglycemic, and neuropsychological activities. All parts of the neem plants are used to treat itching, burning sensation, blood morbidity, and skin ulcers. Steroids, alkaloids, flavonoids, fatty acids, carbohydrates, and terpenoids are some of the various phytochemicals found in Azadirachta indica. Neem has been used safely and effectively for more than 5000 years in India to support the treatment of many common skin disorder such as acne, melasma and heal skin lesions. Neem leaf extract has been reported to inhibit the growth of Propionibacterium acnes, prevent wrinkles formation, and inhibit the growth of fungal species such as

Trichophyton rubrum, Trichophyton mentagrophytes and Microsporum nanum. Biologically active principles isolated from different parts of the plant include: Azadirachtin, meliacin, gedunin, nimbidin, nimbolides, salanin, nimbin, valassin, meliacin forms the bitter principles of Neem oil, the seed also contain tignic acid responsible for the distinctive odour of the oil.[15] Neem kernels contain 30-50% of oil mainly used by the soap, pesticide and pharmaceutical industries and contain many active ingredients which are together called triterpene or limnoids. The four best limnoids compounds are: Azadirachtin, Salannin, Meliantriol, and Nimbin. Limonoids contain insecticidal and pesticidal activity.

Neem (*Azadirachta indica*) is widely used in traditional medicine due to its strong antibacterial and anti-inflammatory activities. Tulsi (*Ocimum sanctum*) contains essential oils and phenolic compounds that help reduce microbial growth and inflammation. The combination of these herbal ingredients can provide a synergistic therapeutic effect in the treatment of acne. Topical gels are considered an ideal dosage form for dermatological preparations because they are non-greasy, easily spreadable, and provide better drug penetration through the skin. Acne vulgaris is a chronic inflammatory skin disorder that affects the pilosebaceous units of the skin.

Overview of some skin related disorder:

1. Acne vulgaris:



Acne vulgaris is a chronic inflammatory disorder affecting the pilosebaceous unit, typically following a prolonged course. It is commonly triggered during adolescence by *Cutibacterium acnes*, a bacterial species, under the influence of normal circulating level dehydro epiandrosterone. This common skin disorder that can present in both inflammatory and non-inflammatory lesions.

The condition commonly manifests with papules, pustules, or nodules primarily on the face, although it can also affect upper arm, trunks and backs.

The pathogenesis of acne vulgaris involves the interaction of multiple factors that ultimately lead to the formation of its primary lesions, which is known as comedo. Although Acne vulgaris is commonly observed among adolescents, it is not restricted to this age group and can affect individual of various ages.

2. Rosacea:

Rosacea is a common skin condition that causes flushing or long term redness on your face. It also may cause enlarged blood vessel and small, pus filled bumps. Some symptoms may flare for weeks to months and then go away for a while. Rosacea can be mistaken for acne, dermatitis or other skin problems.

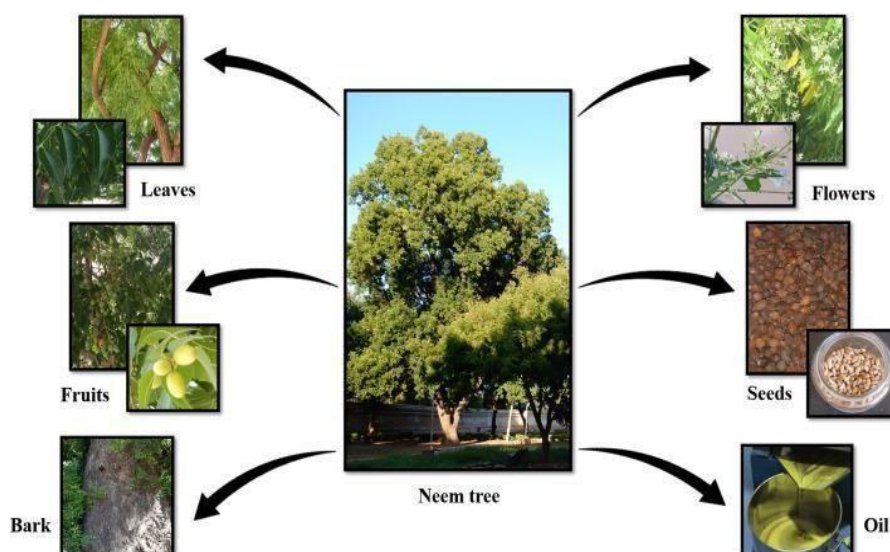
3. Eczema:



Eczema or atopic dermatitis, is the most common form of dermatitis. Many factors, including genetic and environmental factors, are thought to play a part in the pathogenesis of eczema. It is most commonly seen in children but can be seen in adults as well. People with eczema tend to have dry, itchy skin prone to infection. The condition is commonly known as the “itch that rashes” because dry, itchy skin leads to a rash due to scratching or rubbing the skin.

Herbal drug profile:

1. *Azadirachta indica* (Neem):



A. Common name: Neem, Margosa & Indian lilac or commonly called Nimba tree.

Source material; leaves / fruits.

B. Route of administration: oral/ topical.

C. Biological source: It is obtained from the leaves bark or fruits of the *Azadirachta indica* belong to the family meliaceae.

- D. Category:** antibacterial, anti – inflammatory.
- E. Organoleptic characters :**
- Colour – (Bark): dark grey on outside, reddish inside. (Leaves): dark and glossy green.
 - Odour: pungent.
- F. Shape:** (Leaves) - simply pinnate, with leaflets that are ovate to lanceolate, sometime sickle-shaped and slightly serrated.
- G. Chemical constituents:** Insecticidal compound Azadirachtin, bioactive compounds like nimbin, nimbidin, nimbidol and quercetin, limonoids tetranortriterpenoid
- H. Morphological classification of Azadirachta indica:**

Kingdom	Plantae
Order	Rutales
Suborder	Rutinae
Family	Meliceae
Subfamily	Melioidae
Tribe	Melieae
Genus	Azadirachta

I. Uses:

1. Applied topically for skin conditions like eczema, acne and lice.
2. Used in dentistry for reducing plaque and gingivitis.
3. Blood sugar management.
4. Used in agriculture as an eco-friendly pesticides

2. Tulsi Oil:



- A. **Common name:** Holy Basil, Tulasi etc.
- B. **Source material:** leaves
- C. **Route of administration:** oral/ topical.
- D. **Biological source:** It is derived from the fresh and dried leaves and flowering tops of *Ocimum sanctum* Linn.
- E. **Family:** Lamiaceae.
- F. **Category:** Anti-inflammatory, Antiseptic, Aroma Therapy and skin care.
- G. **Organoleptic characters:**
 - a. Colour: typically pale yellow to yellow, greenish-yellow
 - b. Odour: strong, pleasant, spicy, clove-like aroma
 - c. Taste: warm, pungent, slightly bitter
 - d. Texture: smooth, oily
 - e. Volatility: highly volatile essential oil
- H. **Chemical constituents:** Eugenol (60-70), methyl eugenol, beta-caryophyllene, ursolic acid, Rosmarinic acid, Flavonoids, Tannins, and Volatile component.
- I. **Morphological classification of Tulasi oil:**

Kingdom	Plantae
Order	Lamiales
Division	Angiosperm
Family	lamiales
Class	Dicotyledonae

Species	<i>Ocimum sanctum/ Ocimum tenuiflorum</i>
Genus	Ocimum

J. Uses:

1. Anti-acne agent – Helps reduce pimples and skin infections due to its antibacterial activity.
2. Antiseptic and antimicrobial – Used to prevent bacterial and fungal infections.
3. Anti-inflammatory – Reduces redness, swelling, and irritation.
4. Cold and cough relief – Used in herbal remedies for respiratory problems.

Formulation of anti-acne gel:

Sr No.	Ingredients Percentage	Gel 1	Gel 2	Gel 3
1	Azadirachta indica Extract (w/w)	0.45-0.90g	0.30g	0.45g
2	Tulasi oil	1ml	1ml	1ml
3	Carbopol 940	0.36g	0.36g	0.36g
4	Methyl Paraben	0.09g	0.09g	0.09g
5	Propylene Glycol	1.35ml	1.35ml	1.35ml
6	Sodium Hydroxide 10%	q.s	q.s	q.s
7	Rose Water	q.s	q.s	q.s

Materials and Methods:

1. Materials:

The medicinal plants used in the present study include *Azadirachta indica* (neem), *Ocimum sanctum* Linn (tulasi oil). The plant materials were collected from authenticated sources. Carbopol 940 was used as a gelling agent. Other excipients such as propylene glycol, methyl paraben, sodium hydroxide and distilled water were used in the formulation.

2. Collection and authentication of plant material:

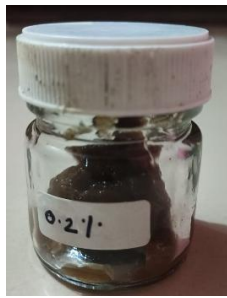
Fresh plant materials were collected from local sources and authenticated based on their morphological and pharmacognostical characteristics. The collected plant parts were washed thoroughly with water to remove dust and impurities and then dried under shade at room temperature.

3. Preparation of plant extract:

1. Neem: Leaves of *Azadirachta indica* and roots of *Rubia cordifolia* were collected from Al-Selw, Taiz. The plant materials were cleaned, washed with distilled water, shade dried for 72 hours, coarsely powdered, weighed, and stored in airtight containers. About 250 g of each powdered material was soaked separately in 1 litre of 95% v/v ethanol for 3–4 days. The mixtures were stirred every 12 hours using a sterile glass rod. The extracts were filtered using Whatman filter paper No. 1. The filtrates were concentrated using a rotary evaporator under reduced pressure at a temperature below 50°C. A dark green residue was obtained and stored in airtight glass jars. The extract weight was recorded and the percentage yield obtained was 10.6%.

4. Stepwise Procedure for Preparation of Gel Formulations:

1. Weigh the required quantity of Carbopol 940 and disperse it in distilled water.
2. Mix the dispersion mechanically using a high-speed mixer until a uniform mixture is obtained.
3. Add 10% Sodium Hydroxide solution slowly with continuous vigorous stirring to neutralize and form the gel base.
4. Place the mixture in a water bath and maintain the temperature below 50 °C.
5. Add *Azadirachta indica* extract in different concentrations to prepare three formulations:
6. Gel-1 : 1% w/w extract
7. Gel-2 : 2% w/w extract
8. Gel-3 : 3% w/w extract
9. Separately dissolve marigold oil and methyl paraben in propylene glycol.
10. Add this prepared solution slowly into the gel base with continuous stirring.
11. Add the remaining quantity of purified water to the formulation.
12. Adjust the pH dropwise using 10% sodium hydroxide solution until the desired pH is obtained.
13. Make up the final weight to 100 g using purified water (q.s.).
14. Stir the final formulation thoroughly to obtain a smooth and homogeneous gel.
15. Transfer the prepared gel into suitable containers and store properly.



Evaluation of Gel formulations:

1. **Physical appearance:** The gel formulations were evaluated for their physical parameters like colour, odour, consistency, transparency, and homogeneity.

A. Colour: A visual inspection was conducted to determine the formulation colour.

B. Consistency: Consistency was evaluated by applying the formulation onto the skin.

C. Odor: The formulation odor was tested by smelling the odor of the mixture of the gel with water.

2. **Measurement of pH:** pH of the formulation was determined by using pH meter. In this method, electrode was washed with double distilled water, dried with the help of tissue paper and then dipped in 20ml gel formulation. The pH of the gel formulations was recorded at ambient condition

3. **Homogeneity:** Once the gels have been established in a beaker, the homogeneity is examined visually to see if any aggregates or gritty materials are present

4. **Spreadability:** A glass slide with standard dimensions was used, where 0.5 g of gel was placed in a circle 1 cm in diameter on the glass slide, over another glass slide was placed. A weight of 125 g was set for 5 min so that the gel was sandwiched between the two slides to form a thin layer. Then, the weight was removed and extra gel was removed. Then the slides were adjusted so that the upper slide was fixed with a weight of about 20 g. The time was noted for the slides to separate from each other.

$$S = M \times L / T$$

Where, M = weight tied to upper slide L = length of glass slides

T = time taken to separate the slides

4. Grittiness:

The prepared formulations of gel were microscopically observed to find out the presence of any unwanted particulate. All the formulations of gel were determined for fulfill the obligation of free from unwanted particulate matter

5. Extrudability Study:

The gel formulations were filled in standard capped collapsible aluminium tubes and sealed to the end. The extrudability was determined by pressing of the thumb

6. Viscosity measurement:

Viscosity of gel was measured by use of Brookfield viscometer. The sufficient quantity of herbal gel was filled in sample holder separately. The height of the gel was filled in the sample holder should sufficiently allow to dip the spindle. Viscosities of the gels were recorded by adjusting the rotating speed of the spindle at 2.5 rpm

7. Antibacterial Activity of Gel formulations:

Each formulation was assessed for its antimicrobial effects against the microorganisms on a nutrient agar using a suitable diffusion method. About 0.2 ml of the bacterial test strain was inoculated over a nutrient agar plate with a sterile cotton swab and was allowed to dry. With the help of a cork borer, 6 mm diameter wells were created. Half a mililitre of the *Azadirachta indica* extract was introduced into the wells.

The plates were placed at room temperature for about one hour. Then the plates were placed in an incubator at 30°C for 24 hour. Then, the zone of inhibition was checked and recorded. Clindamycin was used as standard.

9. Acne Healing Activity of Gel Formulations:

Adults aged from 17 to 22 year old were divided into three groups, having 4 adults each. Group 1, 2 and 3 received Gel-1 containing 1% w/w of the *Azadirachta indica* extracts, Gel-2 containing 2% w/w *Azadirachta indica* extract, and Gel-3 containing 3% w/w of the *Azadirachta indica* extract. No other medicine was given to the adults during the entire study was evaluated for 15 days.

Result and discussion:

1. Physical Parameters Evaluation Of Gel Formulation:

parameter	Gel-1 (1%)	Gel-2 (2%)	Gel-3 (3%)
colour	Green	Dark Green	Dark Green
consistency	Smooth	Smooth	Smooth
grittiness	Free from gritiness	Free from gritiness	Free from gritiness
homogeneity	Homogenous	Homogenous	Homogenous
Apperance	Greasy Transparent	Greasy Transulcent	Greasy Transulcent

2. Skin Irritation Test:

All the gel formulations were found to be safe while being applied on the skin and there was no irritation or sensitivity to the skin.

3. Measurement of pH: :

pH of the formulation was determined by using Digital pH meter.

Property	Standard Range	Gel 1	Gel 2	Gel 3
pH	5.5 – 7.0	6.06	6.16	6.34

4. Mearsurment Spreadability:

The spreadability indicates the extent to which the gel readily spreads on application to the skin or the affected part

Property	Gel 1	Gel 2	Gel 3
Spredability(g.cm/sec)	36	33	31

5. Viscosity Measurment:

Property	Gel 1	Gel 2	Gel 3
Viscosity(cps)	12140	13000	14230

Viscosity of gel was measured by use of Brookfield viscometer.



Viscosity of Gel 1



Viscosity of Gel 2



Viscosity of Gel 3

6. Antimicrobial Activity Of Gel Formulation:

Disc diffusion assay

Table 1. Zone of Inhibition of synthesized compounds against some pathogenic microorganisms

Compound code	<i>E. coli</i>	<i>S. aureus</i>
AA1	2mm	2mm
AA2 Standard	8mm	8mm

NZ=No zo



Conclusion:

The present study successfully formulated and evaluated a herbal anti-acne gel containing *Azadirachta indica* leaf extract using Carbopol 940 as the gelling agent. Three gel formulations containing 1%, 2%, and 3% w/w extract were prepared and evaluated for physical appearance, pH, spreadability, viscosity, skin irritability, and antimicrobial activity. All formulations showed good homogeneity, stability, and acceptable physicochemical properties without causing skin irritation. Among the prepared formulations, Gel-3 containing 3% w/w extract exhibited the highest antimicrobial activity against *Propionibacterium acnes* with a significant zone of inhibition. The study concludes that *Azadirachta indica* herbal gel can be considered a safe, effective, and economical alternative for the management of acne.

References:

1. Zong A, Cao H, Wang F. Anticancer Polysaccharides from Natural Resources: a Review of Recent Research. *Carbohydrate Polymers*. 2012; 90(4): 1395–1410.
2. T. Efferth T, Koch E. Complex Interactions between Phytochemicals. The Multi-Target Therapeutic Concept of Phytotherapy. *Current Drug Targets*. 2011; 12(1): 122–132.
3. Parrotta JA, Chaturvedi A. *Azadirachta Indica* A. Juss. *Neem, margosa*. Meliaceae. Mahogany family. New Orleans: USDA Forest Service, International Institute of Tropical Forestry., 1994; 8.
4. Biswas K, Chattopadhyay I, Banerjee RK, Bandyopadhyay U. Biological activities and Medicinal Properties of *Neem* (*Azadirachta indica*). *curr Sci.*, 2002; 82(11): 1336-45.
5. Puri HS. *Neem: The Divine Tree; Azadirachta Indica*. Amsterdam, the Netherlands: Harwood Academic Publishers. 1999; 183.
6. Maithani A, Parcha V, Pant G, Dhulia I, Kumar D. *Azadirachta Indica* (*Neem*) Leave: A Review. *J Pharm Res.*, 2011; 4(6): 1824-7.
7. Barua C, Talukdar A, Barua A, Chakraborty A, Sarma R, Bora R. Evaluation of The Wound Healing Activity of Methanolic Extract of *Azadirachta Indica* (*Neem*) and *Tinospora Cordifolia* (*guduchi*) in Rats. *Pharmacology online*. 2010; 1: 70-7.
8. <https://www.rxlist.com/supplements/neem.htm>.
9. Osunwoke Emeka A, Olotu Emamoke J, Allison Theodore A, Onyekwere Julius C. The Wound Healing Effects of Aqueous Leave Extracts of *Azadirachta Indica* on Wistar Rats. *J Nat Sci Res.*, 2013; 3(6): 181-6.
10. Jhariya MK, Raj A, Sahu KK, Paikra PR. *Neem-a Tree for Solving Global Problem*. *Indian J Appl Res.*, 2013; 3: 66-8.
11. Gupta AK, Tandon N, Sharma M. *Quality standards of Indian Medicinal Plants*, volume-3, Indian council of medicinal research New Delhi, 2005; 307.
12. Shrotri MK, Ghavane RC, Mukunda U. *Indian Drugs* 2005; 42(1): 20-23.
13. Gupta AK, Tandon N, Sharma M. *Quality standards of Indian Medicinal Plants*, volume-3, Indian council of medicinal research New Delhi, 2005; 315.
14. Sivarajan VV, Balachandran I. *Ayurvedic Drugs and their Plant sources*, Oxford & IBH Publishing Co. Pvt. Ltd., New Delhi, 1994; 292-93.
15. Bechtold T, Mussak R. *Handbook of natural colorants*. John Wiley & Sons Ltd., United Kingdom.

2009; 151-82.

16. Nadkarni KM. Indian Plants and Drugs. Asiatic Publishing House, New Delhi. 1998; 343344.
 17. Joshan RS, Nagarauk R, Anuradha P. Antibacterial properties of extracts of Indian medicinal plants: *Syzygium alternifolium*, *Phyllanthus niruri* *Rubia cordifolia*. Biomed. Pharmacol. J. 2010; 3: 123-128.
 18. Bhatt D, Kumar R, Joshi GC, Tewari LM. Indigenous uses of medicinal plants by the
 19. Vanraji tribes of Kumaun Himalaya. India. J. Med. Plants Res. 2013; 7: 2747-2754
- .Shivangni Rathore, Dr. Shailesh Gupta, Dr. Vivek Gupta (No. 5, 2022) in Journal of Complementary Medicine Research “A Comprehensive Review on Formulation and Evaluation of Herbal Anti-acne Gel”.

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