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Research Article

FORMULATION AND EVALUATION OF AZADIRACHTA INDICA EXTRACT AS ANTIACNE CREAM: A PHARMACEUTICAL DEVELOPMENT STUDY

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Abstract

Background: Acne vulgaris is a multifactorial dermatological disorder affecting pilosebaceous units, with increasing demand for natural therapeutic alternatives due to antibiotic resistance concerns and adverse effects of conventional treatments.

Objective: To formulate and evaluate topical cream preparations containing Azadirachta indica extract for antiacne application, optimizing pharmaceutical parameters for stability, safety, and potential therapeutic efficacy.

Methods: Seven cream formulations (F1-F7) were developed using varying concentrations of neem extract (3-7 mL), beeswax (4-12 g), liquid paraffin, borax, methyl paraben, and lecithin following standard emulsification techniques. Pre-formulation studies included comprehensive extract characterization through organoleptic evaluation and solubility analysis. Formulations were systematically evaluated for physical characteristics, washability, irritability potential, phase separation, homogeneity, and greasiness using established pharmaceutical testing protocols.

Results: Neem extract demonstrated characteristic dark green/brown coloration, strong pungent odor, extremely bitter taste, and preferential oil solubility. Solubility studies revealed free solubility in methanol, solubility in ethanol, high solubility in acetone, and practical insolubility in aqueous systems. Among seven formulations tested, F3 achieved optimal pharmaceutical properties with smooth texture, absence of irritancy, phase separation stability, positive homogeneity, and non-greasy characteristics, scoring 5/5 in comparative evaluation. F4 and F5 demonstrated acceptable properties with scores of 4/5 each.

Conclusion: Azadirachta indica extract can be successfully incorporated into stable cream formulations with favorable pharmaceutical characteristics. Formulation F3 exhibited superior properties suitable for topical antiacne application, warranting further antimicrobial efficacy studies and clinical evaluation.

Keywords: Azadirachta Indica, Neem Extract, Antiacne Cream, Topical Formulation, Pharmaceutical Evaluation, Natural Products

1. Introduction

Acne vulgaris represents one of the most prevalent dermatological conditions globally, affecting approximately 85% of individuals between ages 12-25 years. The multifactorial pathophysiology involves complex interactions between increased sebum production, follicular hyperkeratinization, Cutibacterium acnes colonization, and inflammatory responses. The pathogenesis begins with microcomedo formation, characterized by hyperkeratosis plugs composed primarily of corneocytes in the follicular infundibulum[1][2].

Androgens play a crucial role in acne development, with type I 5-alpha reductase in sebaceous glands converting testosterone to 5-alpha-dihydrotestosterone (DHT), leading to increased sebaceous activity . Acne-associated C. acnes strains demonstrate enhanced capacity to stimulate pro-inflammatory cascades involving TH17 cells, which secrete interferon-gamma and interleukin-17, promoting inflammation . Genetic factors significantly influence sebum composition, with heritability estimates ranging from 50-90%[3].

Current topical antiacne treatments include retinoids, benzoyl peroxide, salicylic acid, and topical antibiotics . However, increasing concerns regarding antibiotic resistance, skin irritation, and systemic side effects have driven interest toward natural therapeutic alternatives . Topical formulations remain cornerstone therapy for mild-to-moderate acne due to direct application minimizing systemic exposure[4].

Azadirachta indica (neem) has demonstrated significant pharmacological properties including antimicrobial, anti-inflammatory, and sebum-regulating activities . The plant contains numerous bioactive compounds including nimbidin, azadirachtin, and other limonoids contributing to therapeutic effects . Previous studies have shown antimicrobial activity against key acne-causing bacteria and anti-inflammatory properties beneficial for acne management[5].

Semisolid dosage forms, particularly creams, offer advantages for topical drug delivery including controlled release, enhanced penetration, and improved patient compliance . Creams as emulsion-based systems can be formulated as oil-in-water (O/W) or water-in-oil (W/O) preparations, with O/W systems generally preferred for non-greasy characteristics and ease of application[6].

The objective of this study was to formulate and systematically evaluate topical cream preparations containing Azadirachta indica extract for potential antiacne application, optimizing formulation parameters to achieve optimal stability and pharmaceutical properties[7].

2. Materials and Methods

2.1 Materials

Fresh Azadirachta indica leaves were collected and processed for extract preparation using standard protocols. Pharmaceutical grade excipients included beeswax (base), liquid paraffin (emollient), borax (alkaline agent), methyl paraben (preservative), lecithin (emulsifier), and rose water. Analytical grade solvents for extraction and characterization included methanol, ethanol, ethyl acetate, and hexane[8].

2.2 Equipment

Analytical procedures utilized Soxhlet extraction apparatus, rotatory vacuum evaporator, Brookfield viscometer, optical microscope, and centrifuge as specified in pharmaceutical compendia[9].

2.3 Extract Preparation and Characterization

Neem leaves were dried, ground, and subjected to Soxhlet extraction with optimization of parameters including solvent selection, temperature, and

extraction time. The concentrated extract underwent comprehensive characterization including organoleptic evaluation and systematic solubility analysis across multiple solvent systems[10].

2.4 Pre-formulation Studies

Extract stability studies evaluated effects of temperature, light exposure, and pH variations. Physical and chemical compatibility between extract and excipients was assessed through standard pharmaceutical testing protocols[11].

2.5 Formulation Development

Seven cream formulations (F1-F7) were prepared using varying concentrations of neem extract and excipients. Standard cream preparation methodology involved separate preparation of oil phase (beeswax, liquid paraffin, lecithin) and aqueous phase (borax, methyl paraben, rose water), followed by controlled emulsification at 65-75°C with continuous stirring using high-shear mixing[12].

2.6 Evaluation Parameters

Formulated creams underwent systematic evaluation for:

- Physical characteristics (color, odor, texture, consistency)
- Washability and protective film formation
- Irritability potential assessment
- Phase separation stability testing
- Homogeneity evaluation
- Greasiness determination
- pH measurement targeting 5.6-5.8 range for skin compatibility
- Viscosity determination using Brookfield viscometer at 100 rpm with spindle #7

2.7 Statistical Analysis

Formulation performance was scored using weighted criteria based on desirable pharmaceutical properties. Each parameter was assigned equal weighting, with total scores ranging from 0-5 points for comparative evaluation[13].

3. Results

3.1 Extract Characterization

Azadirachta indica extract characterization revealed typical neem properties as detailed in Table 1. The extract exhibited dark green to brown coloration, characteristic strong pungent odor, and extremely bitter taste consistent with known neem organoleptic properties.

Table 1. Organoleptic Properties of Azadirachta indica Extract

Parameter	Observed Result
Color	Dark green or brown
Odor	Strong pungent
Taste	Extremely bitter
Solubility	Oil soluble
Texture	Oily and watery distillate

Solubility analysis across multiple solvent systems demonstrated preferential solubility patterns essential for formulation design (Table 2). The extract showed free solubility in methanol, good solubility in ethanol, and high solubility in acetone, while remaining practically insoluble in aqueous systems .

Table 2. Solubility Analysis of Azadirachta indica Extract

Solvent	Solubility
Methanol	Freely soluble
Ethanol	Soluble
Aqueous/water	Practically insoluble
Acetone	Highly soluble
Methyl ethyl ketone	Insoluble

3.2 Formulation Development

Seven formulations were developed with systematic variation in neem extract concentration and excipient ratios to optimize pharmaceutical properties (Table 3). Each formulation utilized standard cream base components with specific functional roles in the final product .

Table 3. Formulation Composition of Cream Preparations

Ingredient	F1	F2	F3	F4	F5	F6	F7	Function
Neem extract	6mL	3mL	5mL	5mL	4mL	7mL	6mL	Active ingredient
Beeswax	10g	7g	9g	12g	10g	5g	4g	Base/emulsifier
Liquid paraffin	3.0g	2.0g	3.0g	3.0g	3.1g	1.5g	2g	Emollient
Borax	2.5g	1.75g	2.0g	1.75g	2.75g	1.75g	3g	Co-emulsifier
Methyl paraben	2.5g	2.0g	2.0g	1.74g	1.75g	1.75g	1.75g	Preservative
Lecithin	0.3g	0.6g	0.6g	0.6g	0.4g	0.6g	0.7g	Emulsifier
Rose water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	Vehicle

Table 4. Comprehensive Evaluation Results of Cream Formulations

Parameter	F1	F2	F3	F4	F5	F6	F7
Physical Evaluation							
Color	White	White	White	White	Cream	White	Cream
Odor	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant
Texture	Uneven	Uneven	Smooth	Smooth	Uneven	Smooth	Smooth
State	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid
Performance Parameters							
Washability	No film	Film formed	No film	Film formed	Film formed	No film	Film formed
Irritability	Irritancy	Irritancy	No irritancy	No irritancy	No irritancy	No irritancy	Irritancy
Phase separation	No separation	Separation	No separation	No separation	No separation	Separation	No separation
Homogeneity	Positive	Negative	Positive	Positive	Positive	Negative	Negative
Greasiness	Positive	Negative	Negative	Positive	Negative	Positive	Negative

3.3 Pharmaceutical Evaluation

Comprehensive evaluation of all seven formulations revealed significant variations in pharmaceutical properties across multiple parameters (Table 4). Physical characteristics assessment showed consistent semisolid consistency across formulations with variations in color, texture, and other critical quality attributes .

3.4 Comparative Performance Analysis

Systematic scoring based on desirable pharmaceutical characteristics identified significant performance differences between formulations. Scoring criteria included smooth texture (+1), absence of irritancy (+1), phase separation stability (+1), positive homogeneity (+1), and non-greasy characteristics (+1), with maximum possible score of 5 points .

Formulation F3 achieved optimal performance with perfect scores (5/5) across all evaluated parameters, demonstrating smooth texture, no irritancy, phase separation stability, positive homogeneity, and non-greasy characteristics. F4 and F5 scored 4/5 each, showing acceptable properties with minor deficiencies. F2 demonstrated poorest performance (1/5) due to multiple quality issues including phase separation and irritancy.

4. Discussion

The successful development of stable Azadirachta indica cream formulations demonstrates the feasibility of incorporating natural extracts into conventional pharmaceutical dosage forms. Extract

characterization confirmed typical neem properties with oil solubility supporting incorporation into emulsion-based formulations, consistent with previous phytochemical studies[14,15].

Formulation F3 exhibited superior pharmaceutical properties attributable to optimal excipient balance. The combination of 5mL neem extract, 9g beeswax, 3.0g liquid paraffin, 2.0g borax, 2.0g methyl paraben, and 0.6g lecithin achieved ideal emulsion stability while maintaining desirable sensory characteristics. The smooth texture, absence of irritancy, phase separation stability, and non-greasy properties make this formulation highly suitable for topical application[16,17].

The observed performance variations across formulations highlight critical relationships between excipient concentrations and final product quality. Higher beeswax concentrations (F4: 12g) maintained stability but introduced undesirable greasiness, while lower concentrations (F6: 5g, F7: 4g) compromised homogeneity and stability. The balanced approach in F3 achieved optimal properties through careful excipient selection and concentration optimization[18,19].

Neem's established antimicrobial activity against Cutibacterium acnes and Staphylococcus aureus supports its potential antiacne application. The anti-inflammatory properties attributed to bioactive compounds including nimbidin and azadirachtin may contribute to reduction in acne-associated inflammation. Additionally, reported sebum regulation and pore-tightening effects address key pathogenic factors in acne development[20,21].

The pH targeting of 5.6-5.8 ensures skin compatibility while maintaining extract stability, critical for both safety and efficacy. Viscosity optimization supports user acceptance through appropriate spreadability and retention characteristics essential for topical products[22,23].

Study limitations include absence of detailed antimicrobial efficacy testing, clinical evaluation data, and comprehensive stability assessment under accelerated conditions. The current work focused on pharmaceutical development and characterization, establishing foundation for future biological and clinical studies[24,25].

The formulation approach employed standard pharmaceutical principles with systematic optimization of critical variables. The emulsification process at controlled temperature (65-75°C) with high-shear mixing ensured uniform particle size distribution and stable emulsion formation . The use of methyl paraben as preservative provides broad-spectrum antimicrobial protection for water-containing formulations[26,27].

Future research directions should include comprehensive microbiological testing against acne-relevant pathogens, in vitro penetration studies, in vivo efficacy evaluation, and extended stability studies under various storage conditions. Clinical trials would be essential to establish therapeutic efficacy and safety profile in human subjects .[28,29]

The successful formulation of neem extract into pharmaceutically acceptable creams contributes to the growing body of research on natural product-based dermatological treatments. This approach aligns with increasing consumer preference for natural alternatives and addresses concerns regarding antibiotic resistance in acne therapy[30,31].

5. Conclusion

This study successfully demonstrates the formulation and evaluation of Azadirachta indica extract as an antiacne cream with favorable pharmaceutical properties. Among seven formulations developed, F3

exhibited optimal characteristics including smooth texture, absence of irritancy, phase separation stability, positive homogeneity, and non-greasy properties, achieving perfect scores in comparative evaluation[32,33].

The systematic approach to formulation development and evaluation provides a robust foundation for natural product-based antiacne therapeutics. The balanced excipient composition in the optimal formulation ensures stability while maintaining desirable sensory characteristics essential for patient compliance[34,35].

The established antimicrobial, anti-inflammatory, and sebum-regulating properties of neem extract, combined with appropriate pharmaceutical formulation design, support the potential development of effective natural antiacne treatments. The results warrant further antimicrobial efficacy studies, clinical evaluation, and comprehensive stability assessment to establish therapeutic potential and commercial viability[36,37].

This research contributes to the expanding field of natural product pharmaceuticals and addresses the growing need for effective, safe alternatives in acne management. The methodology and findings provide valuable insights for formulators working with botanical extracts in topical applications[38].

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8. Conflicts of Interest

The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this paper.

9. References

1. Alexiades-Armenakas M. Aminolevulinic Acid Photodynamic Therapy for Actinic Keratoses/ actinic cheilitis/acne: Vascular Lasers. Dermatol Clin. 2007;25:25-33.[1]
2. Yan HM, Zhao HJ, Guo DY, Zhu PQ, Zhang CL, Jiang YT. Gut-skin axis: Role of purine metabolism in the treatment of psoriasis and atopic dermatitis. Front Immunol. 2018;9:1904.[2]
3. Kim J. Acne Vaccines: Therapeutic Option for the Treatment of Acne Vulgaris? J Invest Dermatol. 2008;128(10):2353-2354.
4. Farrar MD, Howson KM, Bojar RA, West D, Towler JC, Parry J, et al. Genome Sequence and Analysis of a Propionibacterium acnes Bacteriophage. J Bacteriol. 2007;189(11):4161-4167.
5. Beylot C, Auffret N, Poli F, Claudel JP, Leccia MT, Del Giudice P, et al. Propionibacterium acnes: an update on its role in the pathogenesis of acne. J Eur Acad Dermatol Venereol. 2014;28(3):271-278.
6. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. Lancet. 2012;379(9813):361-372.
7. Muhammad Athar Abbasi, Ayesha Kausar, Aziz-ur-Rehman, Hina Saleem, Sadia Muhammad Jahangir, Sabahat Zahra Siddiqui, et al. Preparation of new formulations of anti-acne creams and their efficacy. African Journal of Pharmacy and Pharmacology. 2010;4(6):298-303.
8. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016;74(5):945-973.
9. Alekha Dash, Somnath Singh, Justin Tolman. Pharmaceutics: Basic Principles and Application to Pharmacy Practice. Academic Press; 2013.
10. Saleem S, Muhammad G, Hussain MA, Bukhari SNA. A comprehensive review of phytochemical profile, bioactive for pharmaceuticals, and

pharmacological attributes of Azadirachta indica. Phyther Res. 2018;32:1241-1272.
11. Biswas K, Chattopadhyay I, Banerjee RK, Bandyopadhyay U. Biological activities and medicinal properties of neem (Azadirachta indica). Curr Sci. 2002;82:1336-1345.
12. Subapriya R, Nagini S. Medicinal properties of neem leaves: a review. Curr Med Chem Anticancer Agents. 2005;5(2):149-146.
13. Aulton ME, Taylor KMG. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 4th ed. Edinburgh: Churchill Livingstone; 2013.
14. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia: Lea & Febiger; 1986.
15. United States Pharmacopeia and National Formulary (USP 43-NF 38). Rockville: United States Pharmacopeial Convention; 2020.
16. Indian Pharmacopoeia Commission. Indian Pharmacopoeia 2018. Volume I, II, III. Ghaziabad: Indian Pharmacopoeia Commission; 2018.
17. Lieberman HA, Rieger MM, Banker GS. Pharmaceutical Dosage Forms: Disperse Systems. 2nd ed. New York: Marcel Dekker; 1996.
18. Ansel HC, Allen LV Jr, Popovich NG. Pharmaceutical Dosage Forms and Drug Delivery Systems. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.
19. European Pharmacopoeia Commission. European Pharmacopoeia 10.0. Strasbourg: Council of Europe; 2019.
20. Kharya MD, Shrivastava N, Shrivastava D. Preliminary phytochemical screening of Azadirachta indica. Oriental J Chem. 2009;25(3):671-674.
21. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. 42nd ed. Pune: Nirali Prakashan; 2008.
22. Remington: The Science and Practice of Pharmacy. 22nd ed. Philadelphia: Pharmaceutical Press; 2012.
23. British Pharmacopoeia Commission. British Pharmacopoeia 2020. London: TSO; 2019.
24. Guidance for Industry: Topical Dermatologic Corticosteroids: In Vivo Bioequivalence. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER). 1995.
25. ICH Harmonised Tripartite Guideline. Stability Testing of New Drug Substances and Products Q1A(R2). International Conference on Harmonisation; 2003.
26. Kumar VS, Navaratnam V. Neem (Azadirachta indica): Prehistory to contemporary medicinal uses to humankind. Asian Pac J Trop Biomed. 2013;3(7):505-514.
27. Shishodia S, Sethi G, Konopleva M, Aggarwal BB. A novel sesquiterpene, α-cyperone, inhibits tumor necrosis factor-α-activated nuclear factor-κB: potential role in chemoprevention. Mol Cancer Ther. 2006;5(4):725-735.
28. Patel SM, Venkata Naga KR, Manavalan R, Challabala K. Formulation and evaluation of clotrimazole gels. Indian J Pharm Sci. 2003;65(3):282-285.
29. SaiRam M, Ilavazhagan G, Sharma SK, Dhanraj SA, Suresh B, Parida MM, et al. Antimicrobial activity of a new vaginal contraceptive NIM-76 from neem oil (Azadirachta indica). J Ethnopharmacol. 2000;71(3):377-382.
30. Girish K, Shankara Bhat S. Neem - A green treasure. Electronic Journal of Biology. 2008;4(3):102-111.
31. Fabry W, Okemo P, Ansorg R. Fungistatic and fungicidal activity of east African medicinal plants. Mycoses. 1996;39(1-2):67-70.
32. Walters KA, Roberts MS. Dermatologic, Cosmeceutic, and Cosmetic Development: Therapeutic and Novel Approaches. New York: Informa Healthcare; 2008.
33. Zhai H, Maibach HI. Skin Penetration Enhancement: Methods and Applications. Boca Raton: CRC Press; 2017.
34. Guidance for Industry: Topical Dermatologic Drug Product NDAs and ANDAs—In Vivo Bioavailability, Bioequivalence, In Vitro Release, and Associated Studies. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER). 1998.
35. Sinko PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences: Physical Chemical and Biopharmaceutical Principles in the

Pharmaceutical Sciences. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.
36. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. 6th ed. London: Pharmaceutical Press; 2009.
37. ICH Harmonised Tripartite Guideline. Good Clinical Practice E6(R2). International Conference on Harmonisation; 2016.
38. Newman DJ, Cragg GM. Natural products as sources of new drugs from 1981 to 2014. J Nat Prod. 2016;79(3):629-661.

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