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Formulation, Optimization, and Evaluation of a Polyherbal Emulsion-Based Hair Serum: A Novel Approach for Alopecia Areata Management

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Abstract

➢ ***Background:***

Alopecia areata (AA) is a T-lymphocyte-mediated autoimmune disorder causing non-scarring patchy hair loss, affecting approximately 2% of the global population.[1,2,4] Conventional therapies — corticosteroids, immunosuppressants, JAK inhibitors — carry adverse effects and high relapse rates. Polyherbal cosmeceuticals offer a safer, multi-mechanistic alternative.

➢ ***Methods:***

Five authenticated herbal drugs — Bhringraj (*Eclipta alba*), Neem (*Azadirachta indica*), Manjistha (*Rubia cordifolia*), Green Tea (*Camellia sinensis*), and Brahmi (*Bacopa monnieri*) — were extracted via Soxhlet (ethanol:water, 50:50 v/v). Four O/W emulsion-based serum batches (F1–F4) were evaluated for pH, viscosity, spreadability, drug content, antioxidant activity (H_2O_2 scavenging), and accelerated stability (ICH Q1A).

➢ ***Results:***

Formulation F3 emerged as optimal: pH 5.1 ± 0.1, viscosity 1,850 ± 78 mPa·s, spreadability 6.5 ± 0.10 cm, drug content 100.2 ± 0.8%, and Bhringraj IC_{50} 78.45 µg/mL. F3 was stable at 40°C/75% RH over 30 days, non-irritant in patch testing (n=10), and free of microbial contamination by SCDM sterility testing.

➢ ***Conclusion:***

The polyherbal serum F3 is a promising, safe, and stable topical preparation with synergistic multi-target phytotherapy for alopecia areata, warranting further in vivo and clinical evaluation.

Keywords: *Alopecia Areata, Polyherbal Serum, Eclipta Alba, Azadirachta Indica, Rubia Cordifolia, Camellia Sinensis, Bacopa Monnieri, Emulsion, EGCG, 5α-Reductase.*

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I. INTRODUCTION

➢ *Overview of Herbal Cosmeceuticals*

Herbal cosmeceuticals occupy a rapidly expanding niche at the intersection of cosmetics and pharmaceuticals. The term "cosmeceutical" was introduced by Kligman to describe topical products that exert measurable therapeutic effects through active phytoconstituents.[10,11] Secondary metabolites including flavonoids, terpenoids, alkaloids, and phenolic acids exhibit antioxidant, anti-inflammatory, enzyme inhibitory, and hair growth-promoting properties. Historical documentation — from the Ebers Papyrus to Ayurvedic texts — confirms centuries of plant-based hair care using Bhringraj, Brahmi, and Neem. Contemporary global demand for natural topical serums has renewed

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scientific interest in validating these traditional uses through rigorous pharmaceutical research.[26]

➢ *Hair Biology and the Hair Growth Cycle*

The hair follicle is divided into a permanent upper portion (infundibulum, isthmus, bulge) and a cycling lower portion (suprabulbar region, hair bulb, dermal papilla).[7,8] The dermal papilla (DP), consisting of specialized fibroblast-like cells, communicates with epithelial cells via paracrine signals (IGF-1, VEGF, KGF) to control follicular cycling. The bulge region houses multipotent hair follicle stem cells (HFSCs) responsible for follicular regeneration. The hair growth cycle comprises: Anagen (active growth, 2–7 years); Catagen (regression, 2–3 weeks); and Telogen (resting, ~3 months).[9]

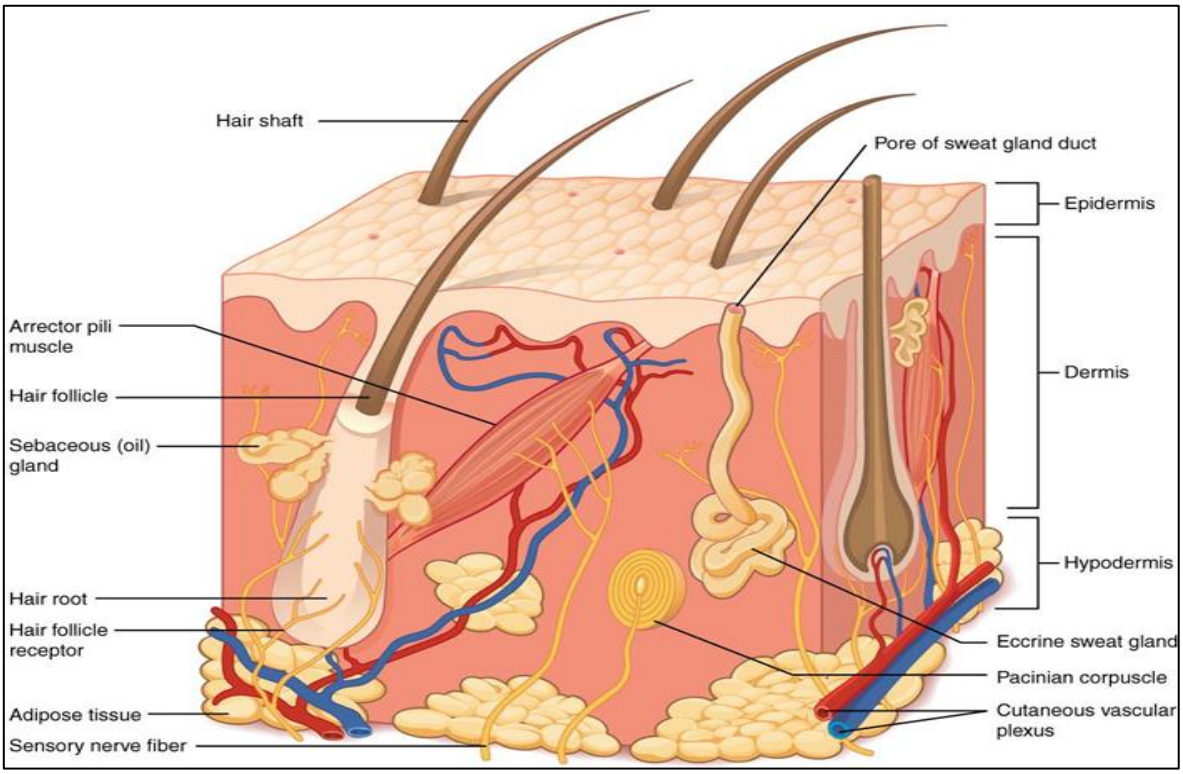

Fig 1 Hair Anatomy Diagram

➢ *Alopecia Areata — Pathophysiology*

Alopecia areata (AA) is an organ-specific, T-cell-mediated autoimmune disorder with non-scarring hair loss affecting approximately 2% of the population worldwide.[2,4,6] The central pathophysiological event is collapse of the immune privilege of the hair follicle. Normally, follicles suppress MHC class I expression and secrete immunosuppressive factors (TGF-β, α-MSH, CGRP). In AA, NKG2D$^+$ CD8$^+$ cytotoxic T cells accumulate around the hair bulb — producing the classic "swarm of bees" peribulbar lymphocytic infiltrate — and release IFN-γ, IL-15, and IL-2, triggering a cytokine storm that disrupts the normal hair growth cycle.[3,4] Clinically, AA ranges from patchy loss to Alopecia Totalis, Universalis, Ophiasis, and Alopecia Barbae.[5]

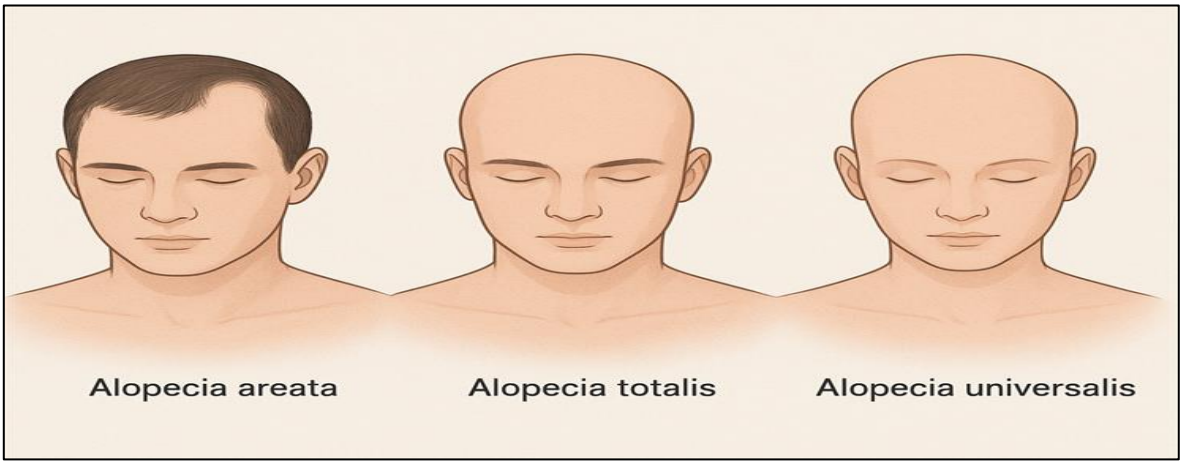

Fig 2 Causes and Pathophysiology of Alopecia Areata

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➢ *Rationale for Polyherbal Emulsion-Based Delivery*

Although individual phytoconstituents demonstrate strong pharmacological activities, their clinical application is restricted by poor aqueous solubility and inadequate follicular penetration.[18] O/W nanoemulsion carriers reduce droplet size to 80–500 nm, enabling surfactant-assisted disruption of the skin's lipid barrier and preferential accumulation in the follicular infundibulum. Encapsulation protects fragile phytoconstituents from oxidative degradation. The five herbs selected in this study offer a rational multi-target approach addressing immunological, oxidative, DHT-mediated, and vascular components of AA simultaneously.[12,17,19]

➢ *Aim and Objectives*

To formulate and evaluate a polyherbal emulsion-based hair serum using extracts of five plants (Bhringraj, Brahmi, Green Tea, Neem, Manjistha) for topical management of Alopecia Areata. Specific objectives include:

- Procure, authenticate, and standardize five herbal crude drugs macroscopically, microscopically, and chemotaxonomically
- Prepare standardized hydroalcoholic extracts via Soxhlet extraction and determine extractive values
- Perform phytochemical screening and TLC fingerprinting of active constituents
- Formulate and optimize four trial batches (F1–F4) using a 3^2 full factorial design
- Assess antioxidant activity, primary skin irritation safety, and sterility (SCDM)
- Conduct ICH Q1A(R2) accelerated stability studies and compare with a marketed serum[26]

II. MATERIALS AND METHODS

➢ *Materials*

Five medicinal plants — *Eclipta alba*, *Bacopa monnieri*, *Azadirachta indica*, *Camellia sinensis*, and *Rubia cordifolia* — were obtained as gift samples from Supriya Lifesciences Limited in dried powder form. Excipients included Polysorbate 20 (O/W emulsifier), Xanthan Gum (viscosity modifier), Glycerin and Propylene Glycol (humectants), Disodium EDTA (metal ion sequestrant), carrier oils (Coconut, Argan, Jojoba, Pumpkin Seed, Caprylic/Capric Triglyceride), Vitamin E Acetate (antioxidant), Caffeine, D-Panthenol, Rosemary Extract, and Phenoxyethanol (preservative). Instruments: Shimadzu UV-1800 Spectrophotometer, Brookfield DV-II$^+$ Viscometer, Systronics Digital pH Meter, and Buchi Rotary Evaporator.

Fig 3 Dried Herbs of all Extracts

➢ *Extraction of Herbal Drugs*

A hydroalcoholic solvent system (ethanol:water, 50:50 v/v) was standardized for all five plants to extract both polar (polyphenols, flavonoids, saponins) and moderately polar compounds (wedelolactone, purpurin, bacosides). Soxhlet continuous hot extraction was the primary method owing to its exhaustive extraction efficiency and reproducibility.[21,23] Each extract was characterized for percentage yield, loss on drying, total ash content, and extractive values per WHO quality control guidelines.[23]

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Fig 4 Soxhlet Process Performed in Lab

➢ *Phytochemical Screening*

Systematic screening for major secondary metabolites was performed on all five dried extracts using standard qualitative chemical tests as per Harborne (1998) and Trease & Evans (2002).

Table 1 Phytochemical Screening Results (+++ Strong ++ Moderate + Weak − Not Detected)

Phytoconstituent	Bhringraj	Neem	Manjistha	Green Tea	Brahmi
Alkaloids — Dragendorff's	+	++	−	+	+
Flavonoids — Shinoda	++	+	+	+++	++
Tannins — $FeCl_3$	++	+	+	+++	+
Saponins — Foam Stability	+	+	+	+	+++
Anthraquinones — Bornträger's	−	−	+++	−	−
Phenolic Compounds — $FeCl_3$	++	+	+	+++	+
Triterpenoids — Liebermann–Burchard	+	++	+	+	+++

➢ *TLC Fingerprinting*

TLC was performed on precoated silica gel 60 F_{254} plates. Rf values were calculated and compared against reported standards for each marker compound.

Table 2 TLC Fingerprinting Data for All Five Herbal Extracts

Extract	Target Marker	Observed Rf	Standard Rf	Detection
Bhringraj	Wedelolactone	0.58 ± 0.03	0.55–0.62	UV 366 nm blue fluorescent band
Neem	Nimbin	0.71 ± 0.04	0.68–0.74	Anisaldehyde H_2SO_4 — brown-red zone
Manjistha	Purpurin	0.43 ± 0.03	0.40–0.47	Orange-red spot (visible)
Green Tea	EGCG	0.52 ± 0.03	0.50–0.56	$FeCl_3$ spray — dark blue-black zone
Brahmi	Bacoside A3	0.38 ± 0.04	0.35–0.42	Anisaldehyde H_2SO_4 — grey-brown band

➢ *Formulation of Polyherbal Serum — Trial Batches F1–F4*

Four O/W emulsion-type trial batches were prepared with varying concentrations of herbal extracts, Xanthan Gum, and Polysorbate 20 using a 3^2 full factorial design. Critical quality attributes targeted: viscosity 1,500–2,500 mPa·s; pH 5.0–5.5; drug content 98–102%.

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Table 3 Quantitative Composition of Trial Formulations F1–F4 (% w/v per 10 mL) — F3 is the Optimized Batch

Ingredient	F1 (%)	F2 (%)	F3 (%)	F4 (%)
Xanthan Gum	0.15	0.20	0.20	0.25
Green Tea Extract	1.0	1.5	1.5	2.0
Bhringraj Extract	0.5	1.0	1.0	1.5
Brahmi Extract	0.5	0.75	1.0	1.0
Manjistha Extract	0.25	0.5	0.5	0.75
Neem Extract	0.25	0.5	0.5	0.75
Polysorbate 20	2.0	2.5	2.5	3.0
Phenoxyethanol	0.985	0.985	0.985	0.985
Glycerin	4.0	4.0	4.0	4.0
Purified Water	q.s.	q.s.	q.s.	q.s.

Fig 5 Trial Samples

Fig 6 Label with Ambered Bottle

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III. RESULTS AND DISCUSSION

➢ *Organoleptic Properties and pH*

Table 4 Organoleptic and Physicochemical Properties of Trial Batches F1–F4

Parameter	F1	F2	F3 (Optimized)	F4
Colour	Golden brown	Brown orange	Amber/Golden brown	Golden orange
Appearance	Slightly turbid	Slightly turbid	Clear and glossy	Clear
pH	5.6 ± 0.1	5.3 ± 0.1	5.1 ± 0.1	4.9 ± 0.1
Viscosity (mPa·s)	980 ± 55	1,450 ± 67	1,850 ± 78	2,320 ± 95
Spreadability (g·cm/s)	35.0 ± 0.8	42.5 ± 0.9	54.2 ± 1.1	48.3 ± 1.0
Phase Separation	Absent	Absent	Absent	Absent

F3 demonstrated the most favourable organoleptic profile with a distinctive amber-golden hue, pleasant herbal aroma, and smooth non-tacky texture. All formulations maintained pH within the physiologically compatible scalp range (4.5–5.5). F3 at pH 5.1 ± 0.1 maintains the hair cuticle in its smoothly closed conformation, preventing hygral fatigue.

➢ *Viscosity and Spreadability*

F3 exhibited mean viscosity of 1,375.3 cP at 25°C/20 RPM, within the acceptable range for hair serum products (500–3,000 cP). The pseudoplastic (shear-thinning) behaviour — viscosity decreasing with increasing RPM (1,484 cP at 10 RPM → 1,226 cP at 50 RPM) — ensures optimal spreadability and scalp adherence. F3 achieved the greatest mean spread diameter (6.5 ± 0.10 cm) and highest spreadability coefficient (54.2 ± 1.1 g·cm/s). F1 failed the acceptance criterion (4.2 cm) due to insufficient oil-phase concentration.

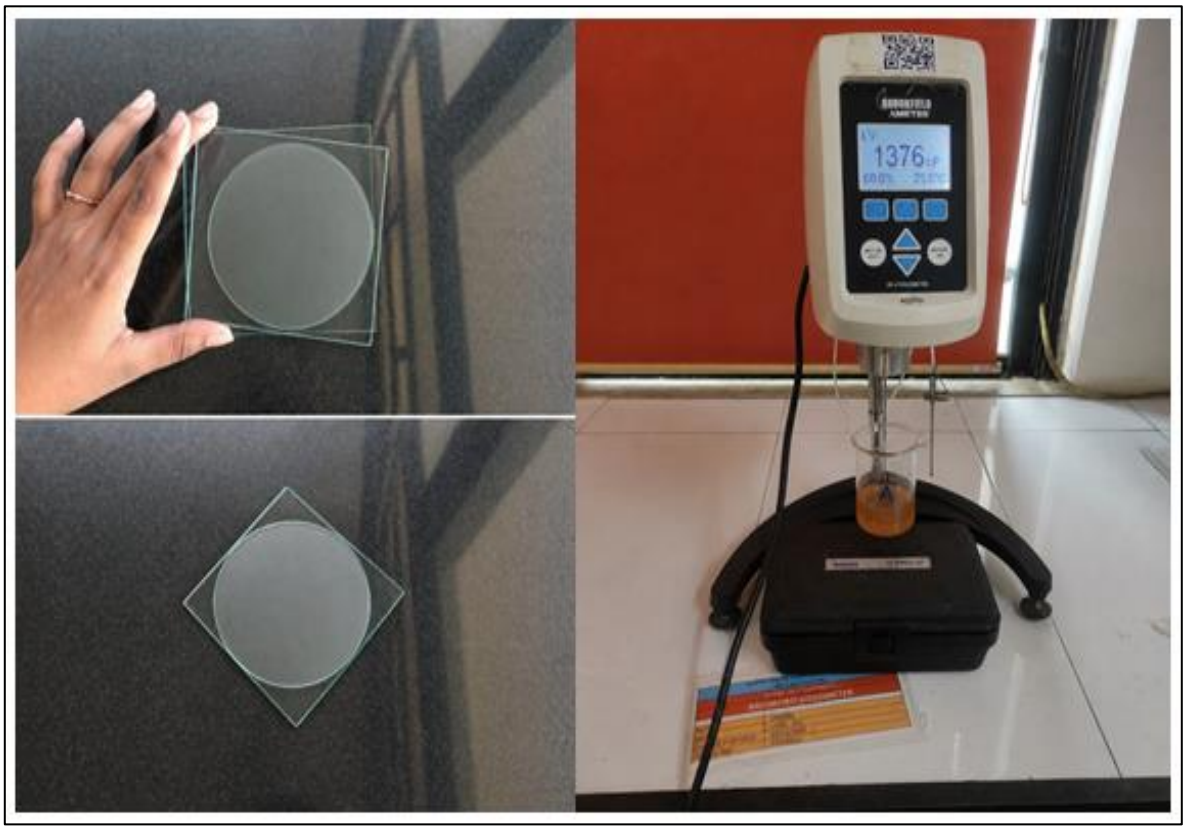

Fig 7 Spredability & Viscosity

➢ *Drug Content and Centrifugation Stability*

Drug content of F3 was 100.2 ± 0.8% by UV-Vis spectrophotometry (λmax 350 nm, wedelolactone as marker), confirming accuracy of the manufacturing process. All four formulations passed centrifugation testing at 3,000–5,000 rpm for 30 minutes with no phase separation, creaming, or cracking, attributed to optimal concentrations of Polysorbate 20 (2.5%) and Xanthan Gum (0.20%) in F3.

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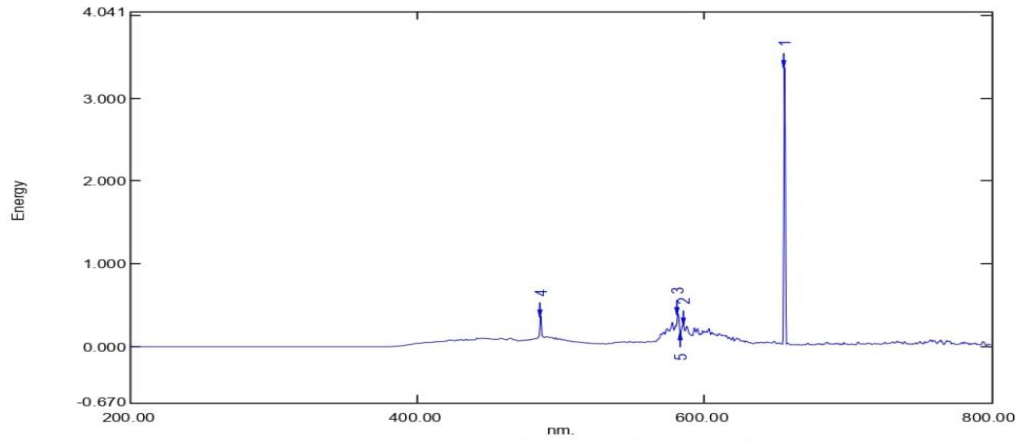

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3	↑	581.50	0.392	
4	↑	486.00	0.368	
5	↓	583.50	0.165	

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Overlay Spectrum Graph Report

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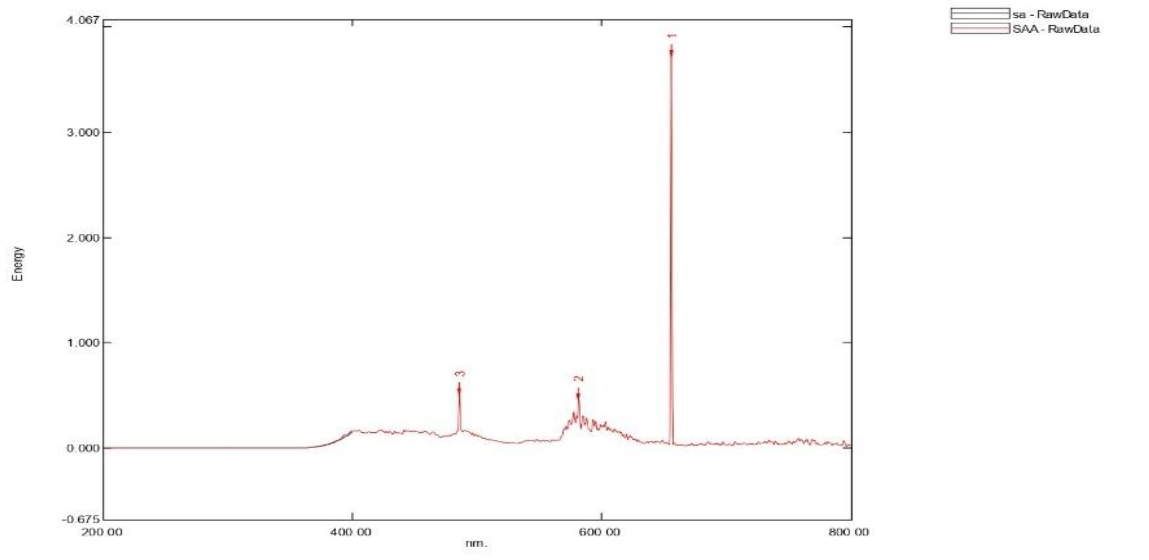

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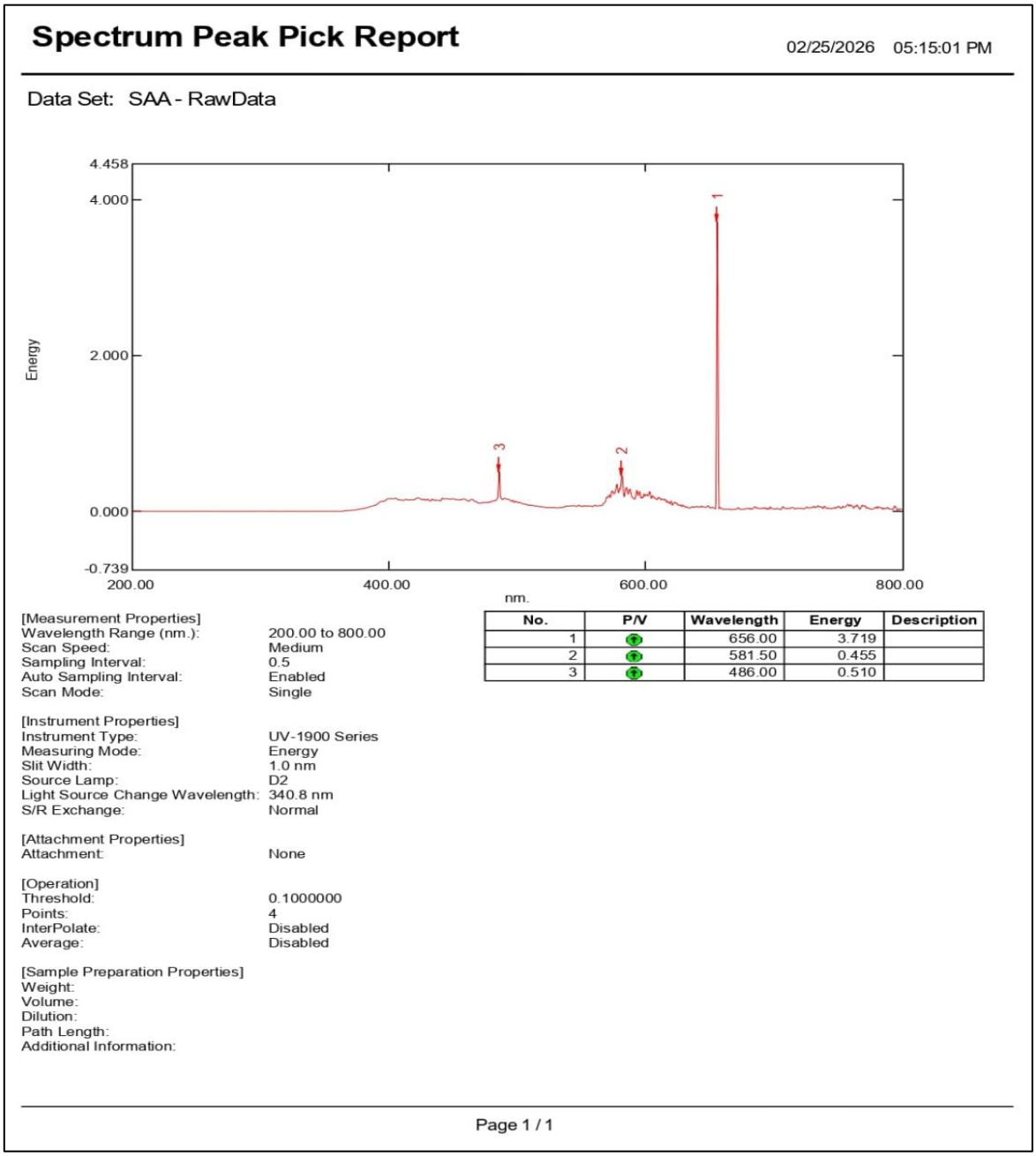

Fig 8 UV Spectroscopy Showing Peaks at 200nm-800nm

➢ *Antioxidant Activity — H_2O_2 Scavenging Assay*

Table 5 H_2O_2 Scavenging Activity of Bhringraj Extract vs. Ascorbic Acid Standard at 230 nm

Concentration (µg/mL)	Bhringraj Abs.	Std (Ascorbic Acid) Abs.	Bhringraj % Scavenging
0 (Blank)	0.850	0.850	—
20	0.660	0.590	22.35
40	0.570	0.480	32.94
60	0.500	0.390	41.18
80	0.430	0.310	49.41
100	0.380	0.240	55.29
IC_{50} (µg/mL)	**78.45**	**46.82**	—

Bhringraj extract demonstrated significant concentration-dependent H_2O_2 scavenging (IC_{50} = 78.45 µg/mL) compared to ascorbic acid standard (IC_{50} = 46.82 µg/mL).[13] Multi-component antioxidant synergy — combining wedelolactone (Bhringraj), EGCG (Green Tea), and bacosides (Brahmi) — represents a significant advantage over single-ingredient preparations in countering ROS-mediated follicular damage in AA.

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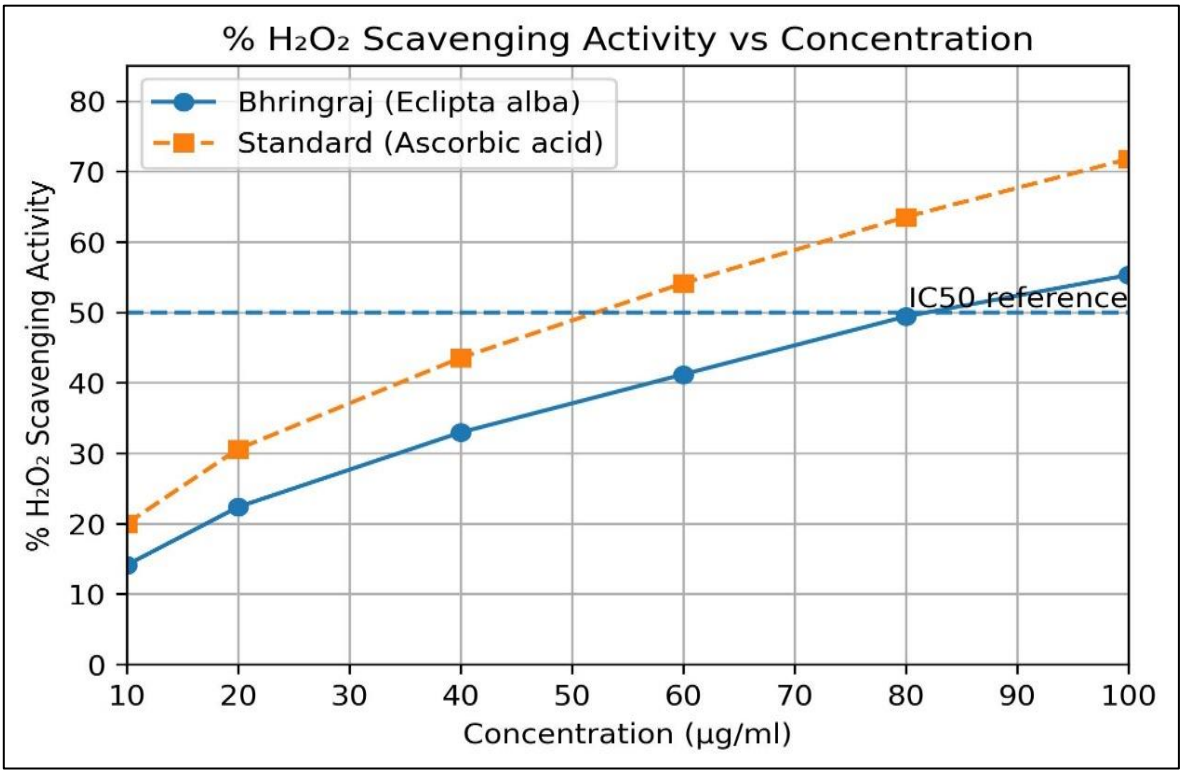

Fig 9 Graph Showing Relationship Between Bhringraj and Standard Solution

➢ *Stability Studies (ICH Q1A(R2))*

Table 6 Accelerated Stability Study — F3 at D0 and D30 (40°C/75% RH, ICH Q1A(R2))

Parameter	Day 0	Day 30	Acceptance Criteria
pH	5.1 ± 0.1	5.1 ± 0.1	4.5–6.5
Viscosity (mPa·s)	1,850 ± 78	1,845 ± 80	1,500–2,200
Drug Content (%)	100.2	99.8	98–102
Colour	Amber brown	Golden brown	Unchanged
Microbial Load	Absent	Absent	Absent
Phase Separation	Nil	Nil	Nil

F3 exhibited outstanding physicochemical stability over 30 days under accelerated conditions (40°C/75% RH) with no significant changes in pH, viscosity, drug content, or microbial load, supporting a projected shelf life of at least 24 months.[24] The minor acceptable colour shift (amber to golden brown) is attributed to progressive oxidation of polyphenolic pigments and is not considered clinically significant.

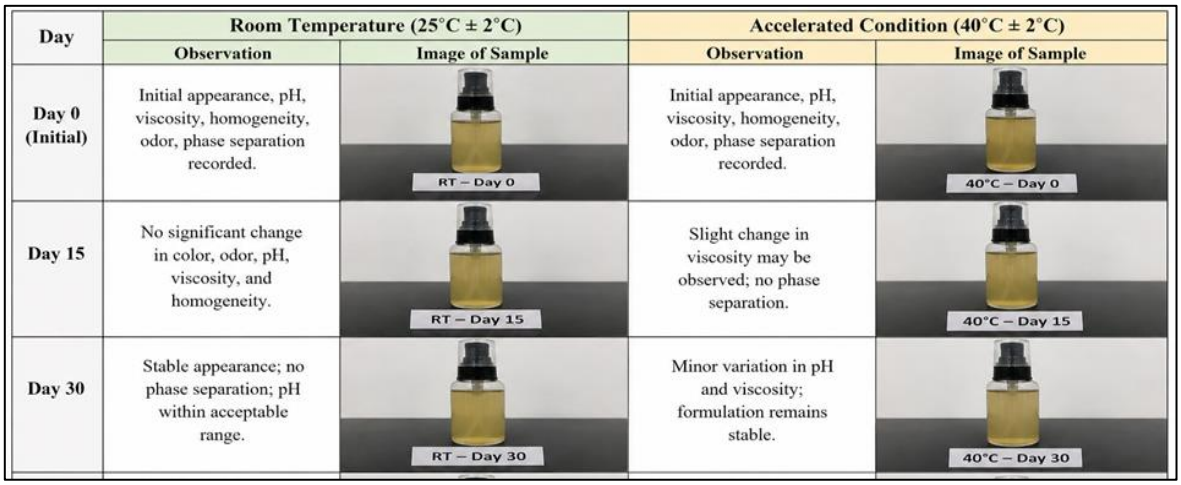

Fig 10 Accelerated Stability Studies Carried on for 30 Days

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➢ *Safety Profile — Patch Test and Sterility Testing*

Primary skin irritation testing on 10 healthy volunteers (0.5 g F3 applied under occlusive patch for 24 hours) showed no redness, itching, swelling, or allergic reaction at 24, 48, or 72 hours, classifying F3 as non-irritant. SCDM sterility testing confirmed absence of viable microbial contamination on Days 3, 5, and 7, validating the efficacy of phenoxyethanol (0.985% w/v) as the preservative system.

Fig 11 Showing Sterility Activity Using SCDM

➢ *Comparison with Marketed Formulation*

Table 7 Comparative Evaluation — F3 Polyherbal Serum vs. Wheezal AloEx Hair Serum

Parameter	F3 Polyherbal Serum	Wheezal AloEx (Marketed)
Formulation Type	Polyherbal O/W emulsion serum	Herbal/Homeopathic hair serum
Main Actives	Bhringraj, Brahmi, Neem, Green Tea, Manjistha	Aloe vera, Jaborandi, Arnica, Cantharis
pH Range	5.1 ± 0.1	Approx. 5.5–6.5
Drug Content	100.2 ± 0.8% (standardized)	Not standardized per plant extract
Antioxidant Activity	High (EGCG + Bhringraj synergy)	Moderate
Patch Test Safety	Confirmed non-irritant (n=10)	CE/regulatory approved

IV. CONCLUSION

The present study successfully formulated and evaluated a polyherbal emulsion-based hair serum incorporating standardized extracts of Bhringraj (*Eclipta alba*), Brahmi (*Bacopa monnieri*), Neem (*Azadirachta indica*), Green Tea (*Camellia sinensis*), and Manjistha (*Rubia cordifolia*) for topical management of alopecia areata. Among four trial batches, formulation F3 — containing 1.0% Bhringraj, 1.5% Green Tea, 1.0% Brahmi, 0.5% Manjistha, 0.5% Neem, and 0.20% xanthan gum — emerged as the optimized formulation.

F3 demonstrated: scalp-compatible pH 5.1 ± 0.1; optimal viscosity 1,850 ± 78 mPa·s with pseudoplastic behaviour; excellent spreadability (6.5 ± 0.10 cm); drug content 100.2 ± 0.8%; confirmed Bhringraj antioxidant IC_{50} of 78.45 µg/mL; ICH Q1A(R2) accelerated stability (40°C/75% RH, 30 days) with a projected shelf life of ≥24 months; non-irritant skin safety (n=10); and SCDM-confirmed sterility.

TLC fingerprinting confirmed all five marker compounds (wedelolactone, nimbin, purpurin, EGCG, bacoside A3) within standard Rf ranges.[21,22] In conclusion, polyherbal O/W emulsion hair serum F3 represents a promising, safe, stable, and scientifically validated topical preparation addressing multiple pathomechanisms of alopecia areata through synergistic phytotherapy. Future work will include in vivo hair growth studies and extended clinical evaluation to further establish F3 as a reliable herbal alternative to conventional immunosuppressant therapies.

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