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ORIGINAL ARTICLE

Safety and efficacy of REGENDIL™ infused hair growth promoting product in adult human subject having hair fall complaints (alopecia)

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Abstract

Background: Hair serum is recommended therapy for the management of hair fall problems. People of all ages suffer from hair fall.

Aim: To evaluate safety and efficacy of hair growth promoting product in healthy adult subjects with hair fall complaints (Alopecia).

Methods: In this safety and efficacy clinical study, 32 healthy individuals (aged 18–45 years) experiencing hair loss were enrolled. Participants applied 0.5 mL of the product to the affected scalp area daily for 60 days. The study evaluated various factors, including hair growth rate, thickness, density, scalp condition using CASLite-Nova, anagen-to-telogen ratio, hair fall reduction, overall hair and scalp appearance, hair strength, and participants' subjective perceptions of the product.

Results: Highly statistically significant improvement was observed in hair growth rate, thickness, and density at Day 30 and Day 60. Hair growth rate increased (p-value <0.01) by 10.52% in 30 days and 31.62% in 60 days after test product application. Average hair growth increased by 424.21 μm/day and 487.31 μm/day at Day 30 and 60 respectively. The hair growth improved by up to 1.5 times after 60 days of usage in healthy subjects with hair fall complaints. No adverse events or product-related adverse events were reported.

Conclusion: Hair serum containing REGENDIL™ (Redensyl, AnaGain, Procapil, Capilia longa), and 5 kDa hyaluronic acid was efficacious and well tolerable in reducing hair fall (Alopecia). Hair serum significantly improved hair growth, hair density, hair thickness, and hair strength within 60 days of usage, thereby demonstrating it worth as a beneficial inclusion as a daily haircare product.

KEYWORDS
alopecia, hair fall, hair growth, hair loss, phototrichogram

1 | INTRODUCTION

Hair fall is a part of natural hair balance and when this balance between natural hair growth and hair fall interrupts, it is known as hair fall. In current scenarios, losing hair is a major problem. Changes in lifestyle, hormonal changes, stress, low nutrient-rich diet, medication, and environmental factors are some of the factors responsible for hair loss. Different types of hair loss patterns are found, like androgenetic alopecia (AGA). Medical conditions such as hypothyroidism, use of contraceptives, and nutrition deficiency cause hair loss in men and women respectively.[1,2] By the age of 70 years, hair loss affects at least 80% of males and 50% of females. The incidence of hair loss increases with age and is most prevalent in Caucasians, followed by Asian and African American populations, and finally in Native Americans and Eskimos. Females after 60 and males after 50 years of age have started losing hairs.[3] The hair growth cycle follows three phases namely the anagen phase (growth phase), catagen phase (transit phase), and the telogen phase (resting phase). In the active phase of the hair growth cycle, the hair follicles produce hair fibers, this phase may take many years. After the anagen phase ends, the catagen phase commences. The catagen phase lasts for few weeks. In this phase, hair follicles lose one-sixth of their diameter and follow the apoptosis phase. During this phase club hair formation takes place which is responsible for hair thinning. The resting phase takes 3–4 months. During this phase hair enters a dormant phase where no hair growth takes place.[4–7] In a healthy scalp, approximately 90% of the hair is growing, 1% or less is going through involution.[5] 100 hair fall count is considered a normal hair fall. The test product used in the study contains plant-based active ingredients namely REGENDIL™ (Redensyl, AnaGain, Procapil, Capilia longa), and 5 kDa Hyaluronic acid (HA).

Redensyl is a combination of hair growth promoting ingredients mainly containing two patented molecules, dihydro quercetin-glucoside (DHQG), and epigallocatechin gallate-glucoside (EGCG2). Both of these molecules are stabilized polyphenols that target the hair follicle outer root sheath (ORS) stem cells and fibroblasts cells of the dermal papilla. Redensyl also contains zinc and glycine, both of which are responsible ingredients for the process of hair metabolism.[8] Procapil, the other active component, comprises of three potent plant-derived elements: oleanolic acid sourced from olive leaves, which obstructs the activities of enzymes 5–1 and 5–2 alpha-reductase; apigenin, which is a flavonoid extracted from peels of citrus fruits that aids in dilating blood vessels; and the peptide glycine-histidine-lysine, crucial for enhancing pro-matrix metalloproteinase activity and fulfilling the hair's metabolic requirements.[9] AnaGain is a water-soluble extract derived from organic pea sprouts (*Pisum sativum L.*), obtained through a process guided by bioassays to encourage hair growth and mitigate hair loss. Pea sprouts are abundant in various nutrients like biotin and L-arginine, along with secondary plant compounds such as isoflavones. These compounds, known to stimulate hair growth in experimental settings, underscore their potential in promoting hair growth.[10] Capilia longa is completely made from Curcuma longa, commonly known as turmeric, which promotes hair growth by working on the epigenetic rejuvenation of hair bulbs and increasing blood circulation in the scalp, ultimately preventing hair loss.[11] HA is an endogenous compound that is perceived from numerous tissues and biological fluids as an isolated component. HA, when administered via different routes exhibit antiwrinkle property, improves skin hydration, nail health, and rejuvenates hair fibers.[12]

The objective of the study was to observe the effect of hair growth-promoting product on hair growth, density, and thickness by taking phototrichogram using CASLite-Nova. The anagen to telogen ratio was measured by trichogram employing a pluck test; hair strength was evaluated by pull test, and reduction in hair fall was evaluated by 60-second hair combing and count test. The general appearance of hair and scalp was evaluated by a dermatologist-trained evaluator under the supervision of a dermatologist. Subject perception about the effect of test product on hair growth was evaluated by using a 5-point scale.

2 | MATERIALS AND METHODS

2.1 | Ethical conduct of the study

The study was approved by the local ethical committee—ACEAS Independent Ethics Committee which is registered at The Central Drugs Standard Control Organization (CDSCO) and The Office for Human Research Protections (OHRP) United States Department of Health and Human Services (US DHHS) with CDSCO registration# ECR/281/Indt/GJ/2017/RR-21 and OHRP US DHHS registration# IRB00011046. The study was conducted in accordance with the declaration of Helsinki (Brazil, October 2013), Good Clinical Practices for clinical research in India 2005, new drugs and clinical trials rules 2019, ICH GCP E6 (R2) guidance on good clinical practice, and with ICMR's National ethical guidelines for biomedical and health research involving human participants, 2017. This clinical study was registered with the Clinical Trial Registry of India (CTRI) with CTRI# CTRI/2022/11/047330.

2.2 | Study design and selection criteria

This was an open-label, single-arm, single-centre, proof-of-concept, prospective, non-comparative, safety and efficacy study in adult human subjects having hair fall complaints (Alopecia) (MedDRA Version: 26.1). A total of 45 subjects aged 18 to 45 years were screened, out of them, 32 subjects were enrolled and 29 subjects (15 females and 14 males) completed the study (Table 1). The total duration of the study was 60 days (+2 days) which includes a total of six visits. Visit 01 was scheduled 4 days before Day 01,

TABLE 1 Demographic data.

Parameter	Statistic	(*N* = 29)
Gender *n* (%)	Female	15 (51.7%)
	Male	14 (48.3%)
Race *n* (%)	Asian	29 (100%)
Age (years)	Mean (SD)	35.8 (5.70)
Weight (cm)	Mean (SD)	61.7 (13.6)
Height (kg)	Mean (SD)	165 (10.1)

Abbreviation: SD, standard deviation.

followed by Visit 2 on Day 01, Visit 3 on Day 27 (+2 Day), Visit 4 on Day 30 (+2 Days), Visit 5 on Day 57 (+2 Days), and Visit 6 held on Day 60 (+2 Days). Potential subjects were screened on the basis of inclusion–exclusion criteria only after obtaining signed written informed consent from them. During the screening period, subjects' well-being, demography, dermatological examination, medical history, and current medications (prescription and over-the-counter) used over the past 4 weeks were recorded. Sixty-second hair count test was performed by a dermatologist-trained evaluator. Dermatologist-trained evaluator was a study personnel having relevant experience in conducting research and qualification as a paramedic, who was trained by a dermatologist regarding the evaluation of subjects using different assessment methods used in this study.[13]

The tattoo was made by trained and qualified study staff of $1 \times 1 cm^2$ area on the subjects' scalp, 30 cm from the tip of the nose to the centre of the vertex area. A permanent marker was used to standardize the location of the assessment and photographs of the same site were captured by digital camera. Subjects' hair growth rate, hair thickness, and hair density were measured at baseline by CASLite-Nova (Catseye Systems & Solutions Pvt Ltd, India).

2.2.1 | Inclusion criteria

The study enrolled healthy adult men and nonpregnant/nonlactating women aged 18 to 45 years who were experiencing hair loss (Alopecia) as determined by the dermatologist. Female participants of childbearing age had to confirm a negative pregnancy test. Subjects were included good overall health based on recent medical history, visibly tanned skin as assessed by a dermatologist, specific hair loss levels (40–50 hair counts for females and 25–30 hair counts for males in a 60-second hair combing test during screening), unwashed and untreated scalps for 5 days, hair that wasn't gray, self-reported hair thinning, willingness to provide written consent, and adherence to the study procedures. The study also included participants who had previously used other hair loss control products but agreed not to use medicated or prescription shampoos, hair care products containing Minoxidil or anti-hair fall agents, or any other hair growth or hair loss treatments during the study. They were willing to use only the test product for the entire study period.

2.2.2 | Exclusion criteria

The study excluded subjects who had a history of severe hair fall due to any clinically significant problems like anemia, thyroid problems, and so forth, along with any dermatological condition of the scalp other than hair loss and/or dandruff, who had priorly used hair fall control or hair growth product within 3 months. Additionally, subjects who had undergone prior hair growth procedures like hair transplant or laser therapy, applied topical hair loss treatment for at least 4 weeks, or received systemic hair loss treatment for at least 3 months before study participation were not considered in the study. Furthermore, subjects with a history of alcohol or drug addiction and those who utilized other marketed hair fall control and/or hair growth products during the study period along with a plan to shave scalp hair during the study period were excluded from the study. Subjects who used chronic oral steroids 3 months before and during the study period along with the subjects with a history or present condition of irritated or visibly inflamed scalp or severe scalp disease or an allergic response to any cosmetic products or any other condition which could warrant exclusion from the study, as per the dermatologist's/investigator's discretion, were excluded from the study. Pregnant or breastfeeding females or females who planned to become pregnant during the study period were not included. Subjects who had a history of chronic illness which may influence the cutaneous state or subjects who participated in other similar cosmetics, devices or therapeutic trials or hair/scalp care products within the last 4 weeks were also not included in the study.

2.3 | Test product

Our test product, ThriveCo Hair Serum 2.0 is researched and developed by Anveya Living Private Limited. It is a blend of active ingredients like REGENDIL™ (Redensyl, AnaGain, Procapil, Capilia longa), and 5 kDa HA. Other ingredients present in the test product include, Aqua, Hamamelis Virginiana Water, PEG/PPG-17/6 Copolymer, Propanediol, Pentavitin, Niacinamide, Pseudozyma Epicola, Prunus Amygdalus Dulcis Oil, Camellia Japonica seed Oil, Argania Spinosa Kernal Oil, Helianthus Annuus Seed Oil, Camellia Sinensis Seed Oil, Hydrolyzed Corn Protein, Hydrolyzed Wheat Protein, Hydrolyzed Soy Protein, Caffeine, Arginine, Rosmarinus officianalis Lead oil, Polysorbate 20, Acrylates/C10-30, Alkyl Acrylate Crosspolymer, Phenoxyethanol, and Ethylhexylglycerin.

All the enrolled subjects were advised to take half dropper (0.5 mL) of the test product and apply it on the affected area of the scalp with the help of a dropper. The test product was applied at night before going to bed consecutively for 60 days.

2.4 | Safety assessments

Subjects were inquired about adverse events (AE) and serious adverse events (SAE) such as erythema, edema, pain, pruritus, urticaria at each clinical visit and were informed to contact the investigator at any time to report the possible AE/SAE.

2.5 | Dermatologist evaluation

Changes in the general appearance of hair and scalp were evaluated by a dermatologist-trained evaluator on Day 01, Day 30, and Day 60 as compared to the baseline visit. Changes in the general appearance of hair were assessed by a standard clinical questionnaire and parameters were categorized accordingly. The questionnaire evaluated hair volume, meaning the amount of hair, by categorizing it to full, medium or small. Similarly, hair density (a measure of number of hair strands growing at each square-inch of the scalp) to dense or thinned/shade, hair reflection (how hair appears when lights is projected on it) to shiny or blunt, hair plasticity (ability of hair to be reshaped, molded, or temporarily changed) to waved or flat, hair shininess (measure of how shiny the hairs look) to poor, average or good and hair smoothness (measure of how smooth and frizz free your hairs are) to poor, average or good.[14] The general appearance of scalp was evaluated in terms of experiencing problems like scalp itchiness, redness, roughness, dryness, and scaliness. This was evaluated using a subjective product perception assessment scale ranging from 1 to 5, with 1 meaning no experience at all and 5 meaning experiencing problems to a large extent.

Sixty-second hair count test (hair combing test) was performed with the aim of discovering a range of hair shedding during a 60-s hair combing period. In this study, the subjects were asked by trained study staff to perform a 60-s hair combing test after providing information on the proper technique to be used. After completion of combing, the counting of shredded hair (coming out from the root with bulb/sheath and broken hair separately) was done by the trained study staff.

2.5.1 | Hair pull test

The hair pull test was done to obtain a semi-quantitative clinical impression about the easy falling of scalp hair. Approximately 60 hair shafts were taken between the thumb and index finger, close to the surface of the scalp skin and pulled firmly, but not forcibly away from the scalp with constant strength along with the hair shaft up to the upper hair tip (Figure 1). Epilated hairs were then counted.

2.5.2 | Hair pluck test

To perform the hair pluck test, hairs were taken from the predefined site on the day of enrolment. Surrounding hairs were fixed with clips, and approx. Thirty hairs were carefully ranged. The locks of hairs were tightly plucked with the forceps/rubber-protected jaws as close as possible to the scalp, to avoid dystrophic and broken hairs, and to pluck miniaturized hairs as well. For pulling the hair, use one hand to keep the scalp stretched, and the other hand to pull hairs rapidly with a unique ample movement in the direction of their emergence. A vigorous massage of hair plucked area was done just after the sampling to relieve the discomfort caused by sampling. Hairs were arranged side by side on a glass slide and taped with transparent adhesive tape. Bulbs were examined at low magnification (40x magnification) with a light microscope or on the screen of a microfilm reader. The number of anagen and telogen hairs was recorded and the Anagen to Telogen (A:T) ratio was calculated. Results (images) and slides were preserved for reference.

FIGURE 1 Hair pull test (used to measure the strength of hairs).

2.5.3 | Phototrichogram (tattoo method)

Phototrichogram is a noninvasive, reproducible technique which involves manual marking of shaved hairs on images taken to target areas on the scalp skin showing hair loss or predefined areas in case of cosmetic evaluation in healthy subjects' scalp. In this study, the reference area was assessed as a 0.50 cm^2 scalp skin area marked with a 0.2 mm wide black micro-tattoo. With this technique, several quantitative parameters were assessed in the test area, which included: (i) hair density, (ii) hair thickness, and (iii) hair growth rate. These parameters were measured at 60× magnification respectively using CASLite-Nova (Catseye Systems & Solutions Pvt Ltd, India).

2.6 | Statistical analysis

Patient demographic details, along with hair growth, anagen to telogen hair ratio, scalp appearance and hair density were analyzed using descriptive statistics. Frequencies and percentages were reported for qualitative variables, while means, medians, standard deviations, minimum and maximum values, and 95% confidence intervals were used to summarize quantitative variables. The significance of continuous variables was assessed using the Wilcoxon signed rank test

and considering a *p*-value of <0.05 as clinically significant. All statistical analyses were performed using R statistical software (Version: 4.2.2).

3 | RESULTS

Results of the study revealed that there was a highly statistically significant increment observed in hair growth rate, hair thickness & hair density from baseline visit on Day 01 (Visit 2) to Day 30 (Visit 4) and Day 60 (Visit 6). Hair growth rate showed a statistical increment of 10.52% (*p*-value <0.01) on Day 30 and of 31.62% (*p*-value <0.01) on Day 60 (Table 2). Similarly, a good significant improvement in hair thickness was observed as shown in Figure 2. A splendid improvement was also observed in hair density (Table 3). Hair thickness improved significantly by 24% with a *p*-value <0.01 at Day 30 and by 34% with a *p*-value <0.01 at Day 60. A similar effect was seen for hair density. Hair density exhibited high statistical significance with an increase of 25% with a *p*-value <0.01 on Day 30 and of 40% with a *p*-value <0.01 on Day 60. There was an improvement in scalp condition seen with a decreased number of subjects ($n=2$) with dry scalp having much keratin. 3.45% subjects had a normal scalp with excellent condition and 55.17% of them had a normal scalp with good condition of hair density and thickness on Day 60 of treatment as compared to baseline (Table 4 and Figure 3). Based on the dermatological assessment it was seen that there was an improvement in hair strength (assessed by pull test) with 100% of subjects having good hair strength on Day 60 of test product usage.

Pluck test results showed the improvement in the anagen to telogen ratio of hairs and ultimately in hair fall (Alopecia) and general appearance of hair. At baseline (Day 01) it was observed that 57% of hairs were in Anagen stage and 43% in Telogen stage (A:T ratio was 4:3), which was improved to 80% of Anagen hairs and 20% of Telogen hairs with A:T ratio 4:1 on Day 60, exhibiting enhancement in the hair growth phase. In this study, the baseline average hair growth rate was 343.17 μm/day which is the normal hair growth rate. At Day 30, the average hair growth rate per day was improved to 424.21 μm/day and at Day 60 it was further improved to 487.31 μm/day (Figure 4). Similarly, a statistically significant reduction in hair fall was observed with every successive visit (Figure 5). Up to 24% and 42% reduction was observed in hair fall at Day 30 and Day 60 respectively, as compared to baseline. As per the dermatologist's evaluation, the test product has shown a significant reduction in existing problems like scalp roughness, scaliness, redness, dryness, and itchiness from the baseline visit to Day 30 and Day 60 (Table 5). Also, none of the subjects experienced any new irritation reactions like redness, dryness, itchiness, or burning sensation on the scalp after test product usage. 100% of subjects stated good about the feeling of non-frizziness of their hair at Day 60 of test product usage. Based on statistical analysis and dermatological evaluation of the general appearance of hair, it was observed that there was a high statistically significant improvement in hair volume, reflection, plasticity, density, shininess, smoothness, and reduction in hair oiliness (Figure 6), with increase in hair frizziness (Figure 7) at Day 60 as compared to baseline. Based on the subjects' perception questionnaire, all the subjects felt that their hair became shiny, soft and silky at a larger to moderate extent after using the test product and also were overall satisfied at a larger to moderate extent with the use of the test product. Based on general wellbeing questionnaire, all the subjects had "normal" as a response to all the asked questions (Table 6). The test product proved to be effective in the reduction of dandruff and flaking. Subjects were inquired about AE/SAE at each visit and were informed to contact the investigator at any time to report the possible AE/SAE. However, no AE/SAE occurred during the study. Therefore, it can be considered that the test product was found to be safe, effective and well-tolerated during the study in the subjects having hair fall complaints (Alopecia).

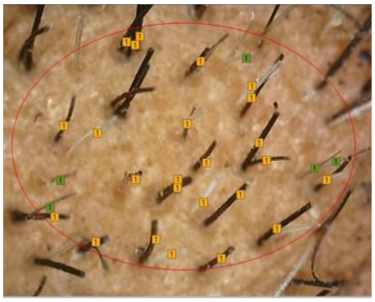
4 | DISCUSSION

The present study successfully determined the safety, tolerability and efficacy of the test product containing REGENDIL™ (Redensyl, AnaGain, Procapil, Capilia longa) and 5 kDa HA as active ingredients that prevent hair loss and stimulate hair growth in both male and female subjects having hair fall complaints (Alopecia). The novelty of the product is the addition of 5 kDa HA, which is a proprietary molecule that has never been introduced to any other hair serum before. It is the smallest form of HA having ultra-low molecular weight which helps it to penetrate rapidly into deep layers of the scalp making the delivery of ingredients precise with maximum impact. This deep penetrating property of low

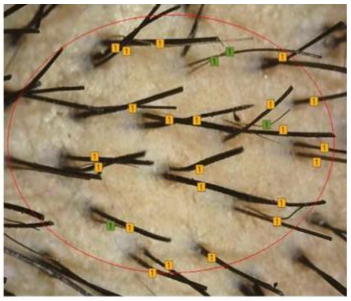
TABLE 2 Change in hair growth rate (μm) as measured by phototrichogram using CASLite-Nova.

Parameter	Statistics	Visit 04 (Day 30)	Visit 06 (Day 60)
Hair growth rate (μm)	*n*	29	29
	%CFB Mean (SD)	10.52 (18.05)	31.62 (38.37)
	Median	6.1	25.52
	Minimum	−9.93	−37.6
	Maximum	81.4	128.09
	p-Value	<0.01	<0.01

Note: % CFB = ((postbaseline - baseline)/baseline) × 100, visit 01 is considered as baseline.
Abbreviation: CFB, change from baseline.



Before Test Product Usage
Hair Density: 236 sq cm
Sub#023: Day 01



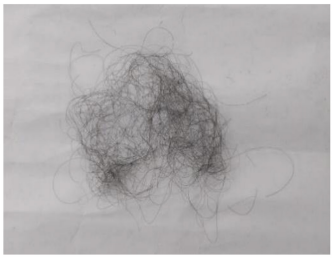
After Test Product Usage
Hair Density: 245 sq cm
Sub#023: Day 60

Before Test Product Usage
Hair Thickness: 17µm
Sub#001, Day 01

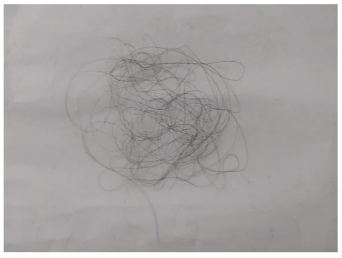
After Test Product Usage
Hair Thickness :20µm
Sub#001, Day 60

Before Test Product Usage
Sub#001, Day 01
Growth Rate: 395 µm/day

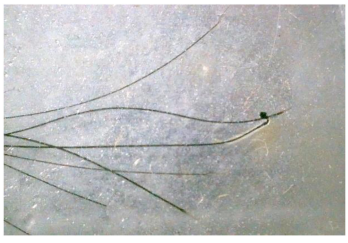
After Test Product Usage
Sub#001, Day 60
Growth Rate: 430 µm/day



Before Test Product Usage
Sub#025, Day 01
Hair Fall: 102



After Test Product Usage
Sub#025, Day 60
Hair Fall: 28



Before Test Product Usage
Sub#001, Day 01
Anagen to Telogen Ratio: 1:5

After Test Product Usage
Sub#001, Day 60
Anagen to Telogen Ratio: 6:1

FIGURE 2 Results of hair thickness, hair density, hair growth, and hair fall measurements—before and after the use of test product.

TABLE 3 Change in Hair Density (sq cm) as measured by phototrichogram using CASLite-Nova.

Parameter	Statistics	Visit 04 (Day 30)	Visit 06 (Day 60)
Hair density (sq cm)	*n*	29	29
	%CFB Mean (SD)	16.79(19.56)	18.43(26.41)
	Median	8.86	11.55
	Minimum	0.3	−18.33
	Maximum	73.74	105.03
	p-value	<0.01	<0.01

Note: % CFB = ((postbaseline−baseline)/baseline) × 100, visit 01 is considered as baseline.
Abbreviation: CFB, change from baseline; sq cm, square centimeter.

TABLE 4 Questionnaire based assessment of change in scalp condition.

Questionnaire	Response	Visit 02 (Day 01)	Visit 04 (Day 30)	Visit 06 (Day 60)
Scalp condition	Dry scalp, dry scalp with much keratin	5 (17.24%)	5 (17.24%)	2 (6.9%)
	Dry scalp, dry scalp with some keratin	8 (27.59%)	9 (31.03%)	10 (34.48%)
	Normal scalp—good condition hair density & thickness	16 (55.17%)	14 (48.28%)	16 (55.17%)
	Normal scalp excellent condition	0 (0.0%)	0 (0.0%)	1 (3.45%)
	NA	0 (0.0%)	1 (3.45%)	0 (0.0%)

FIGURE 3 Scalp condition before and after test product usage.

Before Test Product Usage, Sub#001 - Day 01

(Scalp Condition: Dry Scalp with much Keratin)

After Test Product Usage, Sub#001 - Day 60

(Scalp Condition: Normal Scalp with Good Condition)

FIGURE 4 Baseline and post baseline value of CASLite-Nova hair growth rate (µm).

FIGURE 5 Baseline and post baseline value of 60-s hair count technique (to evaluate reduction in hair fall).

molecular 5KDa HA is the key mechanism for the product's impeccable performance. Redensyl is another active ingredient that is made up of zinc chloride, larix europea wood extract, sodium meta-bisulfite, camellia sinensis leaf extract, glycine, and water. Dihydroquercetin-glucoside (DHQG) and EGCG2 are two active ingredients present in Redensyl. There are multiple modes of action

TABLE 5 Change in scalp appearance.

Parameter	Statistics	Visit 04 (Day 30)	Visit 06 (Day 60)
Itchiness	*n*	29	29
	%CFB Mean (SD)	−20.24 (25.8)	−19.54 (34.52)
	Median	0	0
	Minimum	−66.67	−66.67
	Maximum	0	100
	p-Value	<0.01	<0.01
Redness	*n*	29	29
	%CFB Mean (SD)	−1.79 (34.65)	−15.52 (23.54)
	Median	0	0
	Minimum	−50	−50
	Maximum	100	0
	p-Value	0.299	<0.01
Roughness	*n*	29	29
	%CFB Mean (SD)	−30.95 (24.31)	−59.77 (8.36)
	Median	−33.33	−66.67
	Minimum	−66.67	−66.67
	Maximum	0	−50
	p-Value	<0.01	<0.01
Scaliness	*n*	29	29
	%CFB Mean (SD)	−27.38 (24.52)	−40.8 (21.63)
	Median	−41.66	−50
	Minimum	−50	−66.67
	Maximum	0	0
	p-Value	<0.01	<0.01
Dryness	*n*	29	29
	%CFB Mean (SD)	−8.63 (41.29)	−9.48 (49.89)
	Median	0	0
	Minimum	−66.67	−75
	Maximum	100	100
	p-Value	0.0417	0.0208

Abbreviations: %CFB, percentage change from baseline.

of DHQC as shown by in vitro studies, including activation of hair follicle stem cell division; maintenance of ORS stem cells having an expression of markers such as VDR and K15; initiating pathway of beta catenin and ultimately ORS stem cells differentiation capacity; and boosting of hair follicle dermal papilla fibroblasts metabolism.[8] EGCG2 is known for the prevention and treatment of AGA by selective inhibition of enzyme 5α-reductase activity.[15] Procapil is the combination of three plant-based ingredients: oleanolic acid, a flavonoid extracted from peels of citrus fruits and glycine-histidine-lysine peptide, all of which combinedly help in improving hair growth and metabolism.[9] The results of our study are in line with the pharmacological effects of these ingredients on targeted subjects specifically having complaints of hair loss rather than specific clinical diagnosis of AGA, telogen effluvium as the test product is not indicated for management of specific conditions.

A randomized study was conducted by Karaca et al. including 120 patients from 18 to 55 years of age to compare efficacy of topical 5% minoxidil and a topical preparation of the combination of Redensyl, Capixyl, and Procapil (RCP) for the treatment of AGA. The results of the study showed that the topical preparation of RCP was 64.7% efficacious against AGA compared to 5% minoxidil group, as assessed by the researcher evaluation score Hair recovery in the RCP group was found to be 2.54 times higher than that in the minoxidil group at the end of 24 weeks of treatment.[16]

In another randomization study involving total 54 patient, one treatment group received topical Procapil with Platelet-Rich Plasma (PRP) therapy and other group received topical Redensyl, saw palmetto, and biotin (RSB) with PRP therapy. The results showed that after 6 months both the group showed improvement from baseline of 11.9% in PRP and Procapil (topical) group and of 21.9% in RSB with PRP group.[17] Our study aligns with both these studies where improvement in hair growth had been seen after usage of topical preparation with one or more ingredients similar to our test product.

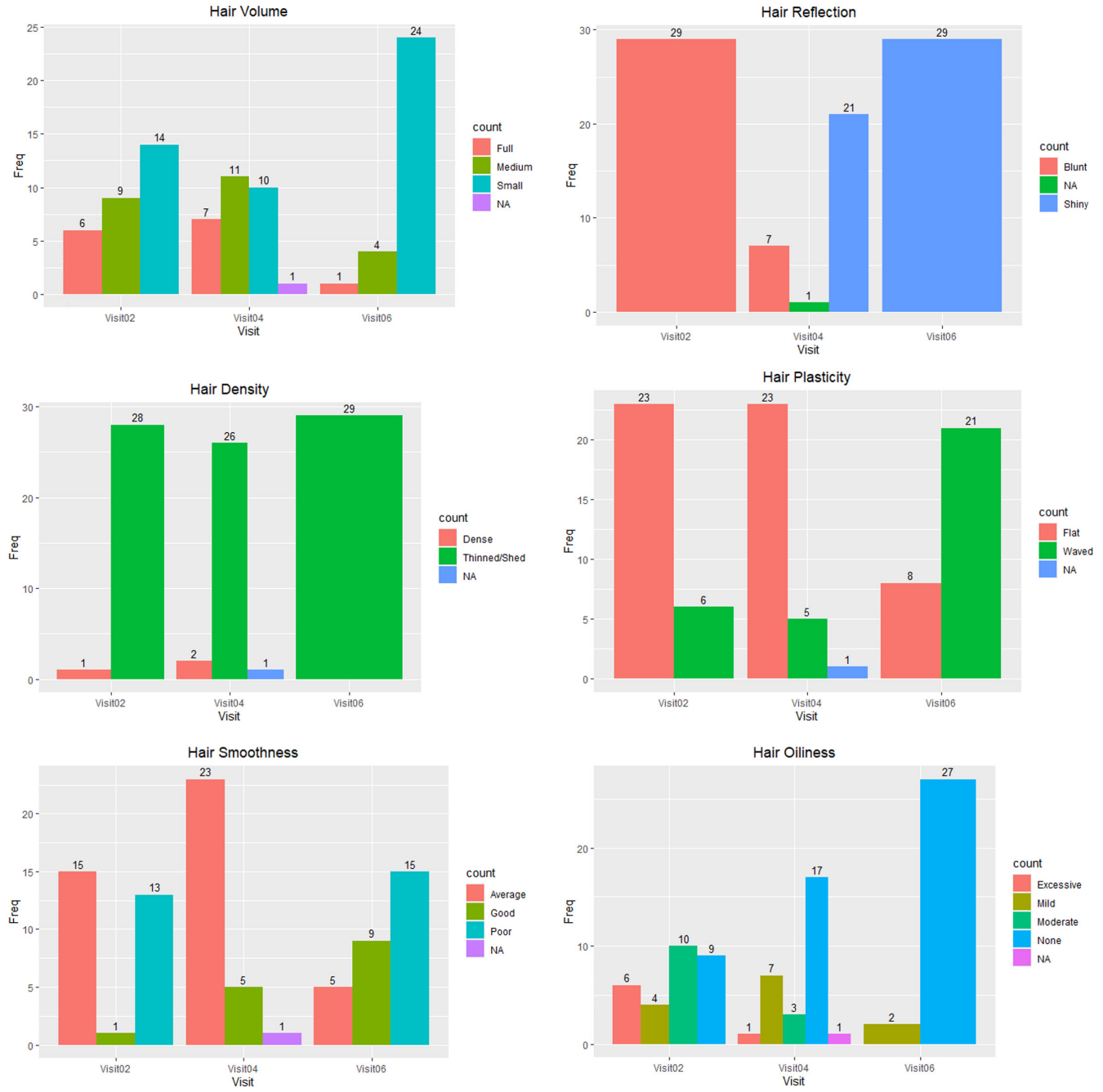


FIGURE 6 Baseline and post baseline comparison of general appearance hair considering hair volume, hair reflection, hair plasticity, hair smoothness, hair shininess and hair oiliness.

In the literature, there are few reports on the clinical efficacy of polyphenols among patients with AGA. In a recent review of the off-label topical treatments for AGA, it was concluded that prostaglandin analogues and polyphenols, such as latanoprost and procyanidin oligomers respectively, can improve hair growth possibly targeting proposed pathogenetic mechanisms of AGA.[18]

AnaGain is another ingredient containing extract of edible organic pea sprouts that are a rich in biotin, L-arginine and isoflavones. Experimental models are suggestive of isoflavones as compounds to promote hair growth.[19]

A pilot study was conducted by Grothe T et al. which demonstrated that the daily supplementation of 100 mg pea sprout extract was safe and effective in decreasing hair loss in patients having hair fall complaints[10] which goes in line with our study.

Other studies reported a significant improvement of terminal hair count in men with hair loss[19] and women with self-reported hair thinning[20,21] upon supplementation of polyphenols.

Various other treatments available are available for hair loss in adults mainly including topical minoxidil and finasteride. However, the use of these drugs does not come without side effects. The most

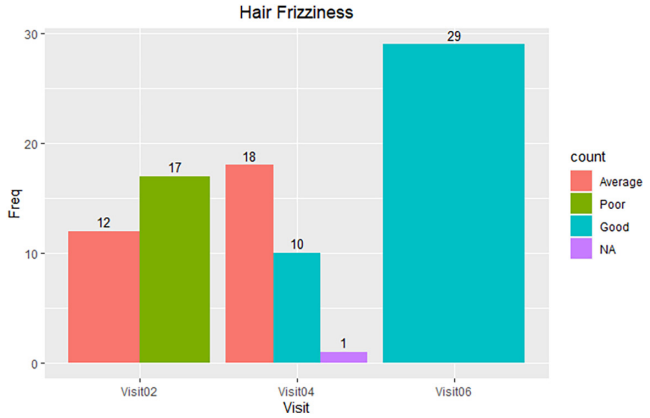


FIGURE 7 Baseline and post baseline value of hair frizziness.

common side effect associated with topical minoxidil use is irritant contact dermatitis which has the characteristic symptoms of scaling and itching.[22] The use of minoxidil in women is associated with facial hypertrichosis.[23] Oral finasteride is also a USFDA-approved drug for the treatment of hair loss. The adverse effects of this drug include gynecomastia, hypersensitivity reactions, dizziness, orthostatic hypotension, testicular pain, and impaired sexual function in males. The drug is contraindicated in pregnant females and females of childbearing potential because of the potential risk of feminization of a male foetus.[24,25] The test product which is made up of a botanical source, was found to be safe with no reported AE as compared to existing pharmaceutical products such as minoxidil and finasteride.

The present study was conducted for a period of 60 days. During this period, we have successfully determined the safety and efficacy of our test product in patients with hair fall complaints. The test product was successful in addressing the complaints of hair fall. Usage of the test product showed a statistically significant increment in hair growth rate, hair thickness & hair density. Additionally, improvements were also observed in hair volume, reflection, plasticity, density, shininess, smoothness, and frizziness while resolving existing problems like scalp roughness, scaliness, redness, dryness and itchiness. The limitation of the study was the lack of a comparative group and lack of sample size. Though the safety and efficacy were proved on small population, the safety and efficacy data on larger populations can be determined to avoid rare or undesirable AE and to study the effect of the product in diverse population.

5 | CONCLUSION

The study's findings are expected to contribute valuable insights to the existing body of knowledge on using hair serums for managing hair loss (Alopecia) concerns. This is particularly significant due to the inclusion of a novel active ingredient, 5 kDa HA, which facilitates rapid ingredient penetration into the deeper layers of the scalp, thereby maximizing the product's impact. Furthermore, after 60 days of use, the hair serum demonstrated effectiveness and good tolerance in improving hair growth, thickness, and strength while reducing hair loss. Importantly, there were no reported adverse reactions such as scalp redness, dryness, itching, or burning sensation in the targeted population experiencing hair loss issues, thereby demonstrating it worth as a beneficial inclusion as a daily haircare product.

TABLE 6 Questionnaire based assessment of general wellbeing.

Questionnaire	Response	*N* = 29, *n* (%)
General health (wellbeing)	Normal	29 (100%)
	Abnormal	0 (0.0%)
Physical appearance	Normal	29 (100%)
	Abnormal	0 (0.0%)
Application site examination by dermatologist trained evaluator	Normal	29 (100%)
	Abnormal	0 (0.0%)
Do you have mild to moderate hair Fall?	Yes	29 (100%)
	No	0 (0.0%)

AUTHOR CONTRIBUTIONS

Conceptualization, Saurav Patnaik, Asrar Ahmed, Shatakshi Maulekhi and Maheshvari Patel; *Data curation*, Saurav Patnaik, and Nayan Patel; *Funding acquisition*, Saurav Patnaik, Asrar Ahmed, Shatakshi Maulekhi; *Investigation*, Apeksha Merja, Nayan Patel and Maheshvari Patel; *Methodology*, Saurav Patnaik, Apeksha Merja, Nayan Patel and Maheshvari Patel; *Project administration*, Saurav Patnaik, Asrar Ahmed, Shatakshi Maulekhi Nayan Patel and Maheshvari Patel; *Resources*, Nayan Patel and Maheshvari Patel; *Software*, Nayan Patel and Maheshvari Patel; *Supervision*, Saurav Patnaik, Shatakshi Maulekhi Apeksha Merja, Nayan Patel and Maheshvari Patel; *Validation*, Apeksha Merja and Maheshvari Patel; *Visualization*, Mr. Saurav Patnaik, Asrar Ahmed, Shatakshi Maulekhi, Nayan Patel and Maheshvari Patel; *Writing* – original draft, Nayan Patel; *Writing – review & editing*, Saurav Patnaik, Asrar Ahmed, Shatakshi Maulekhi Apeksha Merja and Maheshvari Patel.

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CONFLICT OF INTEREST STATEMENT

Dr. Nayan Patel and Dr. Apeksha Merja affirm that they have no conflicts of interest regarding providing scientific insights and designing

the clinical study. Mr. Saurav Patnaik, Mr. Asrar Ahmed and Ms. Shatakshi Maulekhi are employees of Anveya Living Private Limited. Ms Maheshvari Patel was a part of scientific writing and has no conflict of interest. The authors declare that any association has not influenced the work reported in this paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was approved by the local ethical committee- ACEAS Independent Ethics Committee which is registered at CDSCO and OHRP US DHHS. CDSCO registration# ECR/281/Indt/GJ/2017/RR-21 and OHRP US DHHS registration number is IRB00011046. The study was conducted considering the guidelines for Good Clinical Practice (GCP) set forth by the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) as a guide of reference and in accordance with the Declaration of Helsinki regarding the treatment of human subjects in a study. This clinical trial has been registered at the Clinical Trial Registry of India with the trial registered number CTRI/2022/11/047330 [Registered on: 15/11/2022].

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