A randomized, single-blinded, vehicle-controlled study of a topical active blend in the treatment of androgenetic alopecia.

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Abstract

Introduction: Androgenetic alopecia (AGA) is the most common hair disorder, affecting approximately 50% of men and women. A topical lotion that contains two patented formulas (Redensyl® and Sepicontrol A5®), has been introduced as an alternative approach to standard therapies for AGA.

Methods: Forty-four patients with AGA were randomized either to apply the active lotion or the vehicle, twice daily for 24 weeks. Subjects were evaluated at 0, 12, and 24 weeks by clinical examination, photographic documentation, quality of life evaluation (DLQI), and trichogram (anagen to telogen ratio).

Results: Forty-one patients, 18 males and 23 females, completed the study. Among patients receiving active treatment (n=26), 7.7% had great improvement, 73.1% had moderate improvement and 19.2% remained stable. The median self-assessment score increased from 4 at baseline to 6 at 24 weeks ($p<0.001$), while the DLQI improved from 4 to 3, respectively ($p<0.001$). The median anagen to telogen ratio increased from 2.25 to 4.00 to 6.02 at week 0, 12 and 24, respectively. No significant adverse events were reported.

Conclusion: This new topical active blend is effective in the treatment of AGA, with high degree of patients' satisfaction, improvement of quality of life, and an excellent safety profile. Thus, it may represent a useful alternative therapeutic approach for AGA.

Introduction

Androgenetic alopecia (AGA) or pattern alopecia is the most common type of alopecia affecting up to 80% of Caucasian men and up to 50% of women in the course of their life (Kanti, 2018; Goren, 2018). In the United States, the National Institute of Health estimates that 50 million men and 30 million women suffer from AGA (Gupta, 2015). In males, AGA starts as early as in the second or third decade; forty-five percent will present noticeable alopecia by age 35, reaching 65% by the age of 60 years. In females, up to 13% of premenopausal women reportedly have some evidence of AGA, but the incidence increases greatly after menopause, affecting 50 to 75% of women by the age of 65 (Piraccini, 2014; Rogers 2008, Blume- Peytavi, 2011). AGA has a profound impact on self-image and emotional well-being, significantly impairing health-related quality of life (Kanti, 2018).

AGA results from the combined effect of genetic and hormonal factors, leading to a patterned, non cicatricial alopecia that involves the androgen-dependent areas of the scalp. Micro-inflammation, extrinsic and intrinsic factors have been implicated as well in its pathogenesis. AGA is characterized by the shortening of the anagen phase, reduced anagen to telogen ratio and gradual conversion of thick, pigmented terminal hairs into fine, non-pigmented vellus hairs, through the process of follicular miniaturization (Kanti, 2018; Piraccini, 2014; Rogers 2008, Blume- Peytavi, 2011).

The pattern of hair loss differs in males and females. In men, AGA produces a bitemporal recession of the frontal hairline, followed by diffuse thinning at the vertex and the crown (Hamilton-Norwood pattern; Piraccini, 2014). In women, the frontal hairline is preserved and diffuse thinning is observed at the parietal region of the scalp (Ludwig pattern; Norwood, 2000). However, both patterns can be seen in men and women.

Treatment of AGA is challenging. The only FDA approved treatments for AGA are the topical androgen-independent hair growth stimulator minoxidil, either 2% in females or 5% in males (FDA, 1992), and oral finasteride (1mg/d) in males (FDA, 2011).

Minoxidil is the mainstay in the topical treatment of AGA. In a systematic review and meta-analysis, the results showed that minoxidil is more effective than placebo in promoting total and non-vellous hair growth (Gupta, 2015). A significantly higher proportion of patients treated with minoxidil had greater hair growth than patients treated with placebo as judged by both the investigators and patients' self-assessment. Nevertheless, great improvement is observed only in a small subset of patients. In

addition, side effects are not uncommon often leading to discontinuation of therapy. The most common adverse reactions are irritant and allergic contact dermatitis, mostly related to the non-active ingredient propylene glycol. Ectopic (facial) hypertrichosis, episodes of hair shedding due to the synchronization of hair cycle, and, most importantly, loss of the positive effect on hair growth after discontinuation of treatment, have been observed (Rossi, 2012). Therefore, minoxidil is an imperfect therapeutic gold standard.

Other topical treatments for AGA include 5-alpha reductase inhibitors, estrogens, and prostaglandin analogues (Kanti, 2018; Piraccini, 2014; Blumeyer, 2011). In addition, pharmaceutical substances, many of botanical origin, with mechanisms other than antiandrogenic activity, are currently under investigation (Katzer, 2019). Some minimally invasive techniques such as mesotherapy, microneedling and platelet rich plasma (PRP) have shown satisfactory results in selected cases. Among systemic treatments, 5α-reductase inhibitors finasteride and dutasteride, low dose oral minoxidil, and androgen receptor antagonists, such as cyproterone acetate and spironolactone in females, are reported to be the most effective. There are also other therapeutic options: laser hair combs (low level laser therapy), camouflage techniques, and surgical approaches including hair transplantation (Olsen, 2005; DeVillez 1994; Price, 2000; Vexiau, 2002; Whiting 1992). Despite the success of approved therapies, commonly reported side effects and the need for continual use has led to the investigation of alternative therapies (Gupta, 2019). Consequently, there is an unmet need for new safe and effective agents.

Redenyl, a new active blend for topical use, has been introduced for the treatment of AGA. It contains two patented formulas: Redensyl® 3%, Sepicontrol A5® 4%, and Menthol 1.5%. Redensyl® is composed of glycine, zinc chloride, sodium meta-bisulfite, larix europea wood extract, camellia sinensis leaf extract, glycerin and water. As active ingredients it contains two patented molecules, dihydroquercetin-glucoside (DHQG) and epigallocatechin gallate-glucoside (EGCG2), which are two stabilized polyphenols targeting the outer root sheath stem cells and the fibroblasts of the dermal papilla. Glycine and zinc are both involved in the hair metabolism. On the other hand, Sepicontrol A5® contains capryloyl glycine, sarcosine and cinnamonum zeylanicum bark extract. It exhibits several actions including 5α reductase activity and anti-inflammatory effect that might be beneficial in AGA. The complete list of ingredients forming the composition of Redenyl, is shown in Table I.

Aim of the present study was to evaluate the efficacy and safety of this new topical lotion in the treatment of AGA. In addition, we assessed patients' satisfaction with the treatment, as well as the effect of treatment on patients' quality of life.

Materials and Methods

The study was conducted at the 2nd Department of Dermatology and Venereology of the National and Kapodistrian University of Athens, "Attikon" General University Hospital, and at the 1st Department of Dermatology and Venereology of the Aristotle University of Thessaloniki, during a 12-month period (June 2018-May 2019). The design of the study was that of a randomized, single-blinded, vehicle-controlled study. Forty-four unselected patients attending the outpatient clinics of our academic departments, who were clinically diagnosed with AGA, have been recruited. All patients had given their informed consent. The study was approved by the Ethics Committee of our hospitals. Inclusion criteria were the following: male or female sex; age ≥18 years; clinical diagnosis of AGA regardless of clinical pattern and severity; no treatment for AGA, or history of other treatment for any reason that might affect the outcome, during the previous 6 months. Entered patients were randomized (2:1) in a single-blinded manner, using simple randomization. They were assigned to apply either the active lotion or the vehicle, twice daily, for 24 weeks. During the study period, they were not allowed to use any other active agent for AGA, including food supplements. Subjects were evaluated at 0, 12, and 24 weeks by clinical examination, standardized photographic documentation, quality of life evaluation (DLQI) and trichogram. Hair density was assessed by clinical evaluation and comparison of photographs. An improvement of ≤25% was considered as mild improvement, of >25 - ≤50% as moderate, and >50% as great improvement. Quality of life was evaluated using a validated version of DLQI in Greek. For the trichogram, approximately 40 hairs were plugged from the occipital or vertex area of the scalp. The percentage of anagen, catagen, telogen and dystrophic hairs was recorded. The efficacy of treatment was assessed by estimating and comparing the anagen to telogen ratio at week 0, 12, and 24. In the follow-up visits, the participants were asked to grade their level of satisfaction with the treatment in a scale ranging from 1-10. Possible adverse events were also recorded in each follow-up visit.

Statistical analysis

Statistical analysis included descriptive statistics for baseline characteristics of the population. Data are presented as medians and interquartile ranges (IQR), or percentages when appropriate. The primary endpoint of this study is the change of the anagen to telogen ratio from baseline (pre-intervention) to 24 weeks (post-intervention). Secondary endpoints are the change of the anagen to telogen ratio from baseline to 12 weeks, as well as the changes in quality of life, clinical evaluation, and self-assessment from baseline to 24 weeks. Non-parametric tests, namely the two-sample Wilcoxon rank-sum, the matched-pairs Wilcoxon signed-rank, and the chi-squared exact test, that do not require normality, were used for the statistical evaluations. All statistical tests were two-sided. Statistical analysis was carried out using the R software, version 3.5.2. For all the tests, the level of statistical significance was set at 5% ($p<0.05$).

Results

Forty-four patients clinically diagnosed with androgenetic alopecia were randomized (2:1) to receive either active treatment or the vehicle. Of them, forty-one completed the study, twenty-six assigned to the intervention group and fifteen assigned to the control group; three patients, all from the intervention group, did not complete the follow up visits and were excluded from the study. The intervention group (n=26) included 12 males and 14 females, aged 30-60 years (median 44 years). There were 18 cases of female pattern hair loss (FPHL): 15 (57.7%) with Ludwig pattern and 3 (11.5%) with Olsen pattern. There were 9 cases of male pattern hair loss (MPHL) with Hamilton-Norwood pattern (34.6%), all in male patients. In the control group (n=15), there were 6 males and 9 females, aged 31-62 years (median 43 years). Of them, 11 had FPHL: 9 (60%) with Ludwig pattern and 2 (13.3%) with Olsen pattern; and 4 (26.6%) had MPHL with Hamilton-Norwood pattern. The two groups did not differ significantly in terms of their baseline characteristics, except for self-assessment that was better for the control group. The baseline data of the study population, by treatment group, are presented in Table II.

Clinical evaluation

Among the intervention group, 5 patients (19.2%) remained stable, 19 (73.1%) had moderate improvement, and 2 (7.7%) had great improvement in terms of hair density. In contrast, all patients in the control group remained stable (Fig. 1, 2). A statistically

significant difference for any improvement (p<0.001) was documented between the two groups.

Self-assessment

The self-assessment score in the intervention group significantly increased by 2 (2-3) points from 4 (3 – 4) at baseline to 6 (5 – 7) at 6 months ($p < 0.001$). In the control group, the median score was 6 (5 – 6) at baseline and remained unchanged (5 – 6) at 6 months (0, 0–0; $p = 0.68$).

Quality of life

Quality of life was assessed using DLQI; the higher the DLQI score, the more the quality of life is impaired. In patients of the intervention group, DLQI score was reduced from 4 (2 – 7) at baseline to 3 (0 – 5) at 6 months. The median difference from baseline to 6 months was –1 (range –2 to –1; $p < 0.001$). In the control group, the DLQI score increased from 4 (2 – 5) at baseline to 6 (5 – 7) at 6 months. The median difference was +3 (0 to 4; $p = 0.015$).

Anagen to telogen ratio

The anagen to telogen ratio was calculated at baseline, at 3 months and at 6 months. At 3 months, the anagen to telogen ratio significantly increased both in the intervention group (median change: 1.37, IQR: 1.10–1.85; p<0.001), and in the control group (1.5, 1.10–1.65; $p<0.001$). However, this increase did not differ significantly between the two groups ($p=0.81$).

At 6 months, the anagen to telogen ratio was again significantly increased from baseline both for the intervention group (3.40, 3.10–3.85; $p<0.001$) and the control group (1.05, 0.85–1.2; $p<0.001$).The improvement of anagen to telogen ratio between week 0 and week 24, was significantly higher in the intervention group compared to the control group ($p<0.001$).

The results of the statistical analysis for clinical evaluation, self-assessment, quality of life assessment and anagen to telogen ratio, are summarized in Table III. The results were statistically analysed separately for males and females. A statistically sginificant difference was documented for clinical evaluation, self-assessment, quality of life assessment and anagen to telogen ratio, in both genders. These results are also presented in Table III.

Safety assessment

No major topical or systemic adverse reactions were reported during the study period. Few patients from both groups reported mild pruritus on the scalp that, however, did not show any temporal or topographic association with the application of the active lotion or the vehicle.

Discussion

The present study involved patients with AGA regardless of clinical type and severity that were assigned to receive either active treatment with a topical active blend lotion (Redenyl) or the vehicle, twice daily for 24 weeks. According to our results, patients on active treatment showed significantly greater clinical improvement, improved DLQI and self-assessment, and significantly increased anagen to telogen ratio on trichogram, compared to the control group. The improvement was evident at 12 weeks and further improved at 24 weeks. Interestingly, this improvement remained significant when males and females were evaluated separately.

Redenyl is an active blend that combines Redensyl® and Sepicontrol A5®. Redensyl® is a combination of four active ingredients: DHQG, EGCG2, glycine and zinc. Glycine is a major constituent of specific hair proteins called keratin associated proteins (KAP), thus being essential for the hair shaft structure (Rogers, 2004). Zinc is essential for cystine incorporation into keratin. Furthermore, it reinforces hair shaft structure (Hsu, 1971). *In vitro* studies have shown the multiple mode of action of DHQC that includes: activation of hair follicle stem cell division, indicated by the expression of proliferation markers Ki67 and PCN; maintenance of outer root sheath stem cells that express specific markers such as VDR and K15; induction of beta catenin pathway and subsequently outer root sheath stem cells differentiation capacity; anti-apoptotic effect by controlling the expression of Bcl-2 and Bax expression; and boosting the metabolism of the hair follicle dermal papilla fibroblasts. Epigallocatechin3-gallate (EGCG) is a major constituent of polyphenols found in green tea, with potential beneficial effects, such as anti-cancer and anti-oxidant properties. It was suggested it that might be useful in the prevention or treatment of AGA by selectively inhibiting 5α-reductase activity (Kwon, 2007). A study has shown that EGCG promoted in vitro hair growth in hair follicles ex vivo culture and the proliferation of cultured dermal papilla cells. These dual proliferative and antiapototic effects on dermal papilla cells may be mediated by the

upregulation of phosphorylated Erk and Akt and by an increase in the Bcl-2/Bax ratio. Similar results were also obtained in vivo.[20] Additionally, it has been shown *in vitro* that EGCG exhibits anti-inflammatory action by reducing IL-8 released by keratinocytes under inflammatory conditions; as well as an anti-oxidant effect by capturing free radicals (Kwon, 2007; Park, 2013).

Polyphenols phytochemicals possess biological properties in vivo and in vitro that may prove beneficial for certain dermatological conditions, including AGA (Tuong, 2015). On this basis, several topical and oral treatment options have been developed. Animal studies in rodents have shown that animals with spontaneous hair loss that received polyphenol extract from dehydrated green tea in their drinking water for six months, had significant hair regrowth (p=0.014) compared to control animals which received regular water (Esfandiari, 2005). Oral consumption of Annurca apple polyphenolic extracts that are rich in Procyanidin B2, has been demonstrated to promote hair growth and increase hair number, hair weight and keratin growth in healthy human subjects (Tenore, 2018), possibly by inhibiting the pentose phosphate pathway and amino acid oxidation, thus sparing aminoacids for keratin biosynthesis (Badolati, 2018). Common fig (Ficus carica) leaf extract that contains polyphenols produced statistically significant downregulation of VEGF, TNF-α, IL-1α, and 5α-reductase type II in human keratinocyte cells tested by RT-qPCR, compared to the untreated cells (Turcoglou, 2017). These anti-inflammatory and anti-androgenic properties of the fig leaf extract could be used for the topical treatment of AGA.

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. In two studies, procyanidin oligomers showed greater efficacy over the vehicle with response to mean change in hair density at week 24 (p<0.001) (Gupta, 2019).

Cinnamonum zeylanicum bark extract is an active ingredient of Sepicontrol A5®. The dried bark of Cinnamomum verum, which is used in traditional Korean Medicine to improve blood circulation and benign prostatic hyperplasia, has been shown in vitro to suppress protein expression of estrogen receptor α, androgen receptor, 5α-reductase, and steroid receptor co-activator (Choi, 2016). These results suggest that cinnamonum may have a positive effect on androgen-mediated diseases, such as benign prostate

hyperplasia and AGA. Sepicontrol A5® has an anti-5α-reductase activity leading to a reduced DHT synthesis in the pilosebaceous unit. This activity is by 61% higher for Sepicontrol A5 (0.5% m.a.) than zinc gluconate on dermal fibroblasts, and it is significantly ($p<0.01\%$) higher for Sepicontrol A5® (0.1% m.a.) than control and comparable to finasteride (30ng/mL m.a.) (unpublished data). In addition, it produces an anti-inflammatory effect by significantly reducing IL-1α release by stimulated keratinocytes using TLRs agonists and calcium compared to stimulated untreated cells. Furthermore, Sepicontrol A5® exhibits an anti-elastase activity and an anti- free radical activity that is higher than zinc gluconate by 80 % and 44% respectively, as quantified by spectrophotometry, thus protecting the dermal extracellular matrix and reducing the oxidative stress (unpublished data).

To our knowledge, there is no previous published experience with Redenyl or its active ingredients in AGA. Moreover, there are no studies comparing the efficacy of Redenyl with minoxidil. Although topical minoxidil has an excellent safety record, the efficacy remains low. Following daily application of topical minoxidil twice daily for 16 weeks, approximately 40% will regrow hair (Goren, 2018). In a recent systematic review and meta-analysis of the approved treatments for AGA, minoxidil 2% or 5% were superior to placebo ($p<0.00001$). The mean difference in hair count was 14.94 hairs/cm^2 for 5% minoxidil twice daily, and 8.11 hairs/cm^2 for 2% minoxidil twice daily, inferior than finasteride 1 mg daily (18.37 hairs/cm^2), and low-level laser light therapy (LLLLT, 17.66 hairs/cm^2) (Adil, 2018). Among our patients, 80.7% had hair regrowth after 24 weeks treatment with Redenyl, of whom, however, the majority (73.1%) had only moderate improvement.

In conclusion, Redenyl may represent a promising new topical treatment for AGA that is equally effective both in males. It contains active ingredients that promote hair growth possibly by their proliferative and anti-apoptotic effect on dermal papilla cells, as well as by inhibiting 5α reductase. As our results indicate, it is safe and effective, producing significant clinical improvement on both physician assessment and patient self-assessment, and resulting in significantly improved quality of life. These effects are comparable to those reported for the gold standard minoxidil with a better, however, safety profile. Further studies with a larger number of patients, including head-to-head comparison with minoxidil, are needed to establish our early findings. Nevertheless, the multi-dimensional mode of action makes this product a useful addition in our armamentarium, offering an alternative approach for the long-term management of AGA.

Conflicts of interest:

The authors report no conflict of interest.

References

Adil A, Godwin M. (2017). The effectiveness of treatments for androgenetic alopecia: A systematic review and meta-analysis. J Am Acad Dermatol, 77, 136-141.

Badolati N, Somella E, Riccio G, et al. (2018). Annurca apple polyphenols ignite keratin production in hair follicles by inhibiting the pentose phosphate pathway and aminoacid oxidation. Nutrients, 10, 1406.

Blume- Peytavi U, Blumeyer A, Tosti A, et al. (2011). S1 guideline for diagnostic evaluation in androgenetic alopecia in men, women and adolescents. Br J Dermatol, 164, 5-15.

Blumeyer A, Tosti A, Messenger A, et al. (2011). Evidence- based (S3) guideline for the treatment of androgenetic alopecia in women and in men. J Dtsch Dermatol Ges, 9 Suppl 6, S1-57.

Choi HM, Jung Y, Park J, et al. (2016). Cinnamoni cortex (Cinnamonum verum) suppresses testosterone-induced benign prostatic hyperplasia by regulating 5α-reductase. Sci Rep, 6, 31906.

DeVillez RL, Jacobs JP, Szpunar CA, Warner L. (1994). Androgenetic alopecia in the female: treatment with 2% topical minoxidil solution. Arch Dermatol, 130, 303-307.

Esfandiari A, Kelley P. (2005). The effects of tea polyphenolic compounds on hair loss among rodents. J Natl Med Assoc, 97, 816-818.

Goren A, Naccarato T. (2018). Minoxidil in the treatment of androgenetic alopecia. Dermatolog Ther, 31, e12686.

Gupta AK, Charette A. (2015). Topical minoxidil: systematic review and metanalysis of its efficacy in androgenetic alopecia. Skinmed, 13, 185-189.

Gupta AK, Mays RR, Versteeg SG, et al. (2019). Efficacy of off-label topical treatments for the management of androgenetic alopecia. Clin Drug Investig, 39, 233-239.

Hsu JM, Anthony WL. (1971). Impairment of cystine-35S incorporation into skin protein by zinc-deficient rats. J Nutr, 101, 445-452.

Kanti V, Messenger A, Dobos G, et al. (2018). Evidenced based (S3) guideline for the treatment of androgenetic alopecia in women and in men. J Eur Acad Dermatol, 32, 11-22.

Katzer T, Leite Junior A, Beck R, da Silva C. (2019). Physiopathology and current treatments of androgenetic alopecia: Going beyond androgens and anti-androgens. Dermatol Ther, 32, e13059.

Kwon OS, Han JH, Yoo HG, et al. (2007). Human hair growth enhancement in vitro by green tea epigallocatechin-3-gallate (EGCG). Phytomedicine, 14, 551-555.

Norwood O, Lehr B. (2000). Female androgenetic alopecia: a separate entity. Dermatol Surg, 26, 679-682.

Olsen EA, Messenger AG, Shapiro J, et al. (2005). Evaluation and treatment of male and female pattern hair loss. J Am Acad Dermatol, 52, 301–11.

Park SY, Jeong YJ, Sun HK, et al. (2013). Epigallocatechin gallate protects against nitric oxide-induced apoptosis via scavenging ROS and modulating the Bcl-2 family in human dental pulp cells. J Toxicol Sci, 38, 371-378.

Piraccini BM, Alessandrini A. (2014). Androgenetic alopecia. G Ital Dermatol Venereol, 149, 15-24.

Price VH,Roberts JL, Hordinsky M, et al. (2000). Lack of efficacy of finasteride in postmenopausal women with androgenetic alopecia. J Am Acad Dermatol, 43, 768-776.

Rogers GE. Hair follicle differentiation and regulation. (2004). Int J Dev Biol, 48, 163-170.

Rogers NE, Avram MR. (2008). Medical treatments for male and female pattern hair loss. J Am Acad Dermatol, 59, 547-566.

Rossi A, Cantisani C, Melis L, et al. (2012). Minoxidil use in Dermatology: side effects and recent patents. Recent Pat Inflamm Allergy Drug Discov, 6, 130-136.

Tenore GC, Caruso D, Buonomo G, et al. (2018). Annurca apple nutraceutical formulation enhances keratin expression in human model of skin and promotes hair growth and tropism in a randomized clinical trial. J Med Food, 21, 90-103.

Tuong W, Walker L, Sivamani RK. (2015). Polyphenols as novel treatment options for dermatological diseases: a systematic review of clinical trials. J Dermatol Treat, 26, 381-388.

Turcoglou M, Pecmezci E, Kilic S, et al. (2017). Effect of ficus carica leaf extract on the gene expression of selected factors in HaCaT cells. J Cosmet Dermatol, 16, e-54-e58.

Vexiau P, Chaspoux C, Boudou P, et al. (2002). Effects of minoxidil 2% vs. cyproterone acetate treatment on female androgenetic alopecia: a controlled, 12- month randomized trial. Br J Dermatol, 146, 992-999.

Whiting DA, Jacobson C. (1992). Treatment of female androgenetic alopecia with minoxidil 2%. Int J Dermatol, 31, 800-804.

Table I. The complete list of ingredients of Redenyl lotion.

	TRADE NAME	**INGREDIENTS**
1	Aqua (Water)	Aqua (Water)
2	Jaguar Excel	Guar Hydroxypropyltrimonium Chloride
3	Citric Acid	Citric Acid
4	Dissolvine GL-47-S	Tetrasodium Glutamate Diacetate, Aqua (Water)
5	Zemea-Propanediol	Propanediol
6	Redensyl®	Glycerin, Aqua (Water), Sodium Metabisulfite, Larix Europaea Wood Extract, Glycine, Zinc Chloride, Camellia Sinensis (Green Tea) Leaf Extract
7	Sepicontrol A5®	Capryloyl Glycine, Sarcosine, Cinnamomum Zeylanicum Bark Extract, Aqua (Water)
8	Oligoidyne-2-Complex	Zinc Aspartate, Copper Aspartate, Manganese Aspartate, Aqua (Water)
9	Euxyl K 712	Aqua (Water), Potassium Sorbate, Sodium Benzoate
10	Solubilisant LRI	PPG-26 Buteth-26, PEG-40 Hydrogenated Castor Oil, Aqua (Water)
11	Plantacare 810	Caprylyl/ Capryl Glucoside, Aqua (Water)
12	Menthol	Menthol Crystals
13	Alcohol 95°	Alcohol Denat, Aqua (Water)

Table II. Baseline clinical and epidemiological characteristics of patients by treatment group.

	Intervention group (n=26)	Control group (n=15)	Comparison between groups
Age, years	44 (30-60)	43 (31-62)	p=0.81
Disease, duration	9.5 (6-12)	5 (4-15)	p=0.25
Anagen to telogen ratio at baseline	2.25 (1.95 – 2.65)	2.15 (1.95 – 2.45)	p=0.44
DLQI at baseline	4 (2 – 7)	4 (2 – 5)	p=0.69
Self-assessment at baseline	4 (3 – 4)	6 (5 – 6)	p<0.001
Ludwig pattern	15 (57.7)	9 (60)	p=0.88
Olsen pattern	3 (11.5)	2 (13.3)	p=0.87
Hamilton-Norwood pattern	9 (34.6)	4 (26.6)	p=0.60

Data are shown as medians (interquartile ranges) or as *n* (%) when appropriate. The two-sample Wilcoxon rank-sumand the chi-squared exact test were used for comparison of the variables between the treatment groups

Table III. Summary statistics for pre- and post-treatment clinical evaluation, self-assessment, DLQI, and anagen to telogen ration, by treatment group, as well as by gender.

	Intervention group (n=26)	Control group (n=15)	Comparison between groups
Clinical Evaluation			
Stable	5 (19.2)	15 (100)	p< 0.001
Males	2 (7.7)	6 (40)	p=0.02
Females	3 (11.5)	9 (60)	p=0.001
Moderate improvement	19 (73.1)	0 (0)	p< 0.001
Males	9 (34.6)	0 (0)	p=0.015
Females	10 (38.4)	0 (0)	p=0.007
Great improvement	2 (7.7)	0 (0)	p=0.39
Males	1 (3.8)	0 (0)	p=0.63
Females	1 (3.8)	0 (0)	p=0.63
Self assessment			
At baseline	4 (3 – 4)	6 (5 – 6)	
At 6 months	6 (5 – 7)	6 (5 – 6)	
Change from baseline to 6 months	2 (2 – 3); $p < 0.001$	0 (0 – 0); $p = 0.68$	p< 0.001
Males	2 (2 – 3)	0 (0 – 0)	p< 0.001
Females	2 (2 – 2)	0 (0 – 0)	p< 0.001
DLQI			
At baseline	4 (2 – 7)	4 (2 – 5)	
At 6 months	3 (0 – 5)	6 (5 – 7)	
Change from baseline to 6 months	–1 (–2 to –1); $p < 0.001$	3 (0 to 4); $p = 0.015$	$p < 0.001$
Males	-1 (-2 to -1)	4 (2-6)	p=0.002
Females	-1 (-2 to 0)	1 (0-4)	p=0.003
Anagen to telogen ratio			
At baseline	2.25 (1.95 – 2.65)	2.15 (1.95 – 2.45)	
At 3 months	4.00 (3.45 – 4.35)	3.55 (3.45 – 3.85)	
Change from baseline to 3 months	1.37 (1.10 – 1.85); p<0.001	1.50 (1.10 – 1.65); p<0.001	p=0.81
Males	1.32 (0.67-1.70)	1.52 (1.35-1.60)	p=0.70
Females	1.42 (1.15-2.2)	1.50 (1.10-1.65)	p=0.34
At 6 months	6.02 (5.25 – 6.30)	3.15 (3.00 – 3.40)	
Change from baseline to 6 months	3.40 (3.10 – 3.85); p<0.001	1.05 (0.85 – 1.20); p<0.001	p<0.001
Males	3.70 (3.22-3.95)	1.07 (0.84-1.15)	p=0.001
Females	3.3 (2.95-3.65)	1.05 (0.90- 1.20)	p<0.001

Data are shown as medians (interquartile ranges), or as n (%) when appropriate. For the in-group (paired samples) comparison of variables the matched-pairs Wilcoxon signed-rank was used. The two-sample Wilcoxon rank-sum and the chi-squared exact test were used for comparison of the variables between the treatment groups,

Figures 1, 2. The photographic documentation of our patients before and after 24-week application of the active lotion shows a clinical improvement.