Double Blind Clinical Trial for Androgenetic Alopecia: Topical Treatment With The Treatment Product of the Invention A Standardized 7.5% Herbal Extract Preparation

Twenty-four healthy male subjects with Stable III–IV androgenetic alopecia were enrolled in a randomized, double-blind, parallel vehicle-controlled study to confirm the effectiveness and safety of a topically applied, standardized herbal preparation (the treatment product of the invention) cream 7.5 wt. % used once daily in the treatment of androgenetic alopecia.

Androgenetic alopecia is the most common cause of hair loss affecting one third of both men and women. In preliminary studies, the treatment product of the invention, a standardized herbal extract in a vehicle, produced encouraging results as a hair growth agent. In one pilot study, all 18 subjects showed increased hair counts, averaging 119%. A very high percentage (50–100%) of conversion from vellus to terminal hair, and hair remelanization (50–100%) was observed.

Materials and Method

Study Design and Medications

The treatment product of the invention is a standardized 7.5 wt. % herbal extract in a cream base vehicle. The extract is standardized by replicative methods, including standardization against specific compounds which appear naturally in the extract.

A double-blind, placebo-controlled trial was conducted to compare the effect of the treatment product of the invention on hair growth in males with androgenetic alopecia against its placebo vehicle. Patients applied the cream to the scalp daily, at approximately 24 hour intervals, for 40 weeks and were seen in the clinic for efficacy and evaluation every 4 weeks throughout the study.

Twenty-four healthy male subjects under the age of 55 were selected for the study. The average age of the participants in the active group was 45.6 years versus 40.5 years for the placebo group. All subjects had State III–IV androgenetic alopecia. Eight subjects had excessive hair loss. The initial evaluation included health history, physical exam and evaluation of the alopecia condition. Any subjects with underlying diseases or subjects using systemic drugs (e.g., steroids, anti-hypertensives, cytotoxic compounds, vasodilators, anti-convulsant drugs, beta blockers, spironolactone, cimetidine, cyclosporine, anti-depressants) were excluded from the study. Each subject was tattooed with a permanent ink on their vertex area, creating a one centimeter triangle. The hair in the triangle was collected and the subjects entered an 8 week baseline period evaluation before beginning treatment.

Using a randomized, double-blind protocol, the subjects were given either the treatment product of the invention or a placebo of vehicle only. Both the active and the placebo groups were each randomly assigned four subjects with excessive hair loss. Subjects washed their hair daily with shampoo and applied the treatment product of the invention cream to the scalp daily, leaving the cream on for twenty-four hours. Subjects were followed every four weeks and had their hair collected six times at eight week intervals (eight weeks at baseline and an additional forty weeks of follow-up).

Assessment Procedures

Two the commonly used methods of evaluating hair growth are:

(1) counting the hair on the scalp in a marked area and (2) various photographic techniques. Both methods can have a large margin of error due to the difficulty in counting hair on the scalp and the possibility of photographing a bent hair shaft and counting it as two hairs. To avoid these problems a more accurate method for evaluating hair growth was employed, based on a protocol developed by Price (Dermatol., 95:683–687, 1990). The hair growth evaluation included: total hair count, terminal (non-vellus, melanized, mature) hair count, hair length, and total hair weight.

Each subject was tattooed with permanent ink at three points on their vertex area creating a one centimeter triangle. After rinsing the hair of the permanent site with water and soap, the hair was washed with acetone to remove any debris that could change its weight. The hair from the triangle was collected using great care to harvest only within the marked area.

The hair collected was placed on white paper, counted and then divided into terminal hair and vellus hair. The terminal hairs were then counted. The ten randomly selected hairs were also measured for length as part of the evaluation.

The total weight of all the hair samples collected were measured on an analytical scale using the same paper, on the same day, to avoid variations in temperature and humidity.

Results

Efficacy results demonstrate that the treatment product of the invention cream, used once daily, is more effective than the placebo cream vehicle in the treatment of androgenetic alopecia. The initial and final measurements of the active and placebo groups are presented in Table II and Table III below. Table IV compares the average percentage change from baseline of the total hair count, terminal hair count, total hair weight, and average hair length of the ten sample hairs, between the group treated with the product of the invention and the placebo-treated group.

After 40 weeks, 70% of the subjects in the active group had greater than a 30% increase in total hair count, compared with 16% of the subjects in the placebo group. The average total hair count for the group treated with the composition of the invention increased by 77.4%, compared to a 3% increase for the placebo treated subjects (average p value=0.005) (FIG. **1**). 90% of the subjects in the active group had greater than a 30% increase in terminal hair counts, compared with 33% of the subjects in the placebo group. The average terminal hair count for the group treated with the composition of the invention increased by 169.4% over the same period, as compared to a 33.9% increase for the placebo treated group (average p=0.001) (FIG. **2**). The average total hair weight of the active group increased by 49.3% compared to a 20.5% increase for the placebo group (p value=0.16). All the subjects in the active group had increased total hair weight, whereas 41.6% of the subjects in the placebo group had decreased total hair weight. The average hair length change for the 10 randomly selected hairs was 29.8% for the active group and 21.7% for the placebo (p=0.50).

No local irritation, sensitization or other adverse effects were observed or reported in either the active or placebo groups.

TABLE II

ACTIVE GROUP

Subject	AA1	AA2	AA8	AA11	BB1	BB2	BB3	BB7	BB8	BB13
Initial Measurements										
Total Hair Count	51	84	29	7	86	63	5	47	75	23
Terminal Hair Count	32	34	18	2	33	42	4	28	48	8
Hair length-cm (8 Weeks)	1.3	1.6	1.28	0.29	1.72	1.72	1.6	1.12	1.91	1.51
Hair Weight-gm (8 wks)	.001	.0022	.0011	.00029	.0016	.00185		.0021	0.0032	.00137
Final Measurements										
Total Hair Count	89	128	76	17	84	70	4	92	108	72
Terminal Hair Count	73	94	68	9	46	58	4	70	89	44
Hair Length-cm (8 wks)	1.98	1.66	1.82	0.45	1.92	2.49	1.51	1.76	2.71	1.44
Hair Weight-gm (8 wks)	.0016	.00232	.00258	.004	.0018	.0035		.00267	.00489	.0017
Results										
Total Hair Count Change	38	44	47	10	−2	7	−1	45	33	49
% Total Hair Count Change	75%	52%	162%	143%	−2%	11%	−20%	96%	44%	213%
Terminal Hair Count Change	41	60	50	7	13	16	0	42	41	36
% Terminal Hair Count Change	128%	176%	278%	350%	39%	38%	0%	150%	85%	450%
Hair Length Change-cm	.68	.06	0.54	.16	0.2	.77	−0.09	.64	.8	−0.07
% Hair Length Change	52%	4%	42%	55%	12%	45%	−6%	57%	42%	−5%
Hair Weight Change-gm	.0006	.00012	.00148	.00011	.0002	.00165	0	.00057	.00169	.00033
% Hair Weight Change	60%	5%	135%	38%	13%	89%		27%	53%	24%

TABLE III

PLACEBO GROUP

Subject	AA5	AA7	AA12	AA19	BB4	BB5	BB6	BB9	BB10	BB11	BB12	BB15
Initial Measurements												
Total Hair Count	40	44	104	34	42	43	88	45	62	67	59	98
Terminal Hair Count	30	21	46	22	14	27	48	18	46	40	17	62
Hair length-cm (8 wks)	1.5	1.32	1.61	1.11	1.61	1.34	1.7	0.87	1.75	1.74	1.52	1.8
Heir Wgt-gm (8 wks)	.001	.0011	.0019	.0018	.0013	.0013	.0024	.0013	.0025	.003	.0022	.0042
Final Measurements												
Time followed (wks)	40	32	40	40	40	40	40	24	32	40	40	40
Total Hair Count	36	56	112	33	66	24	118	39	64	61	58	92
Terminal Hair Count	30	38	54.	24	34	18	86	18	57	36	29	78
Hair Length-gm (8 wks)	1.39	1.94	2.35	1.64	1.79	0.97	1.71	1.47	2.17	1.61	2.22	1.99
Hair Weight-gm (8 wks)	.0006	.0024	.0029	.00142	.0021	.00098	.00432	.0014	.0031	.0025	.0024	.0036
Results												
Total Hair Ct. Chg	−4	12	8	−1	24	−19	30	−6	2	−6	−3	−6
% Total Hair Ct. Chg	−10%	27%	8%	−3%	57%	−44%	34%	−13%	3%	−9%	−5%	
Terminal Hair Ct Chg	0	17	8	2	20	−9	38	0	11	−4	12	16
% Terminal Hair Ct Chg	0%	81%	17%	9%	143%	−33%	79%	0%	24%	−10%	71%	26%
Hair Length Change-cm	−0.11	0.62	0.74	0.53	0.18	−0.37	0.01	0.6	0.42	−0.13	0.7	0.19

TABLE IV

Average Percentage Change Between The Active Group and Placebo Group

	Average % Change Active Group	Average % Change Placebo Group	T Test P Value
Total Hair Count:	77.4%	3.0%	0.005
Terminal Hair Count:	169.4%	33.9%	0.001
Total Hair Weight	49.3%	20.4%	0.162
Average Hair Length	29.8%	21.7%	0.506

Table IV compares the average percentage change between the active group treated according to the invention and the placebo-treated groups for: total hair count, terminal hair count, total hair weight, and average hair length of ten sample hairs.

Comments

The data from this study clearly demonstrate that the composition cream of the invention, 7.5 wt. %, used once daily, is safe and significantly more effective than the placebo cream vehicle in the treatment of androgenetic alopecia.

The most dramatic increases were seen in total hair counts and in terminal hair counts for the subjects who received the active treatment, compared to those who received the placebo. An excellent correlation was also found between the percentage increase in total hair count and the percentage increase in terminal hair count (FIG. **3**). The correlation coefficient was 0.954 for the active group and 0.947 for the entire study group (1.00 being a perfect correlation). Therefore, counting only terminal hair may be a primary quantitative estimator for hair growth.