Safety and Efficacy of Rice Bran Supercritical CO₂ Extract for Hair Growth in Androgenic Alopecia: A 16-Week Double-Blind Randomized Controlled Trial

Jae-Suk Choi, a,b# Jae Beom Park, a,Jin-Nam Moon, a Sang Wook Son, a,b and Mi-Ryung Kim a

aMajor in Food Biotechnology, Division of Bioindustry, College of Medical and Life Sciences, Silla University; 140 Baegyang-daero, 700 Beon-gil, Sasaeng-gu, Busan 617–736, Republic of Korea; bDepartment of Dermatology, Korea University Ansan Hospital; 123 Jeokgeum-ro, Danwon-gu, Ansan 425–701, Republic of Korea; and cDepartment of R&D, ECOMINE Co., Ltd.; Busan Innobiz Center #402, 1 Mandeok 3-ro, 16 Beon-gil, Buk-gu, Busan 608–736, Republic of Korea.

Received May 6, 2015; accepted August 25, 2015

We conducted a 16-week double-blind randomized controlled single-center trial to evaluate the safety and efficacy of dermal rice bran supercritical CO₂ extract (RB-SCE) in the treatment of androgenic alopecia. Fifty alopecia patients were randomly assigned to the experimental and placebo groups. The experimental group received a dermal application of 0.5% RB-SCE (8 mL/d) to the head skin for 16 weeks while the control group received a dermal application of placebo. Changes in hair count, diameter, and density were evaluated with a Folliscope®. Patient satisfaction was evaluated via questionnaire and clinical photographs were rated by dermatologists. The results showed that RB-SCE significantly increased hair density and hair diameter in male subjects. Patient satisfaction and the evaluation of photographs by dermatologists also confirmed the effectiveness of RB-SCE in the treatment of alopecia. No adverse reactions related to RB-SCE were reported. Therefore, RB-SCE shows promise for use in functional cosmetics and pharmaceuticals.

Key words rice bran supercritical CO₂ extract; hair growth-promoting activity; alopecia; clinical study

A daily loss of about 50–60 scalp hairs is considered normal, but a loss exceeding approximately 100 hairs will result in alopecia. Alopecia has been estimated to affect between 0.2 and 2% of the world’s population.1–3 Although medically viewed as a relatively minor dermatological condition, alopecia may have a significant negative impact on quality of life based on the psychological and symbolic importance of hair.

The demand for drugs that alter hair growth and appearance has spawned a multi-billion dollar industry. To date, only two alopecia treatments, minoxidil and finasteride, have been approved by the U.S. Food and Drug Administration. Topical minoxidil solution (Rogaine for Men and Women; Pharmacia Corp., Peapack, NJ, U.S.A.) has been shown to stimulate new hair growth and to help prevent further hair loss in affected areas in both men and women with alopecia,4,5 although the specific mechanism of action remains unclear. Finasteride (Propecia; Merck Co., Rahway, NJ, U.S.A.) is a synthetic azasteroid that is a potent and highly selective non-competitive antagonist of 5α-reductase type 2. It binds irreversibly to the enzyme and inhibits the conversion of testosterone to dihydrotestosterone.6

Generally, minoxidil is well tolerated for long-term daily use. Side effects of minoxidil are uncommon, but contact dermatitis,7 skin irritation,8,9 dizziness, and tachycardia9 have been reported. Finasteride is also generally well tolerated, with few adverse effects reported over 5 years. In finasteride-treated patients, 1.9% reported loss of libido and 1.4% reported erectile dysfunction in the first placebo. The placebo-treated group reported the same events with frequencies of 1.3 and 0.6%, respectively. These events appeared to resolve on cessation of the treatment and, in some cases, during continued treatment.10 Both drugs were discovered as the result of serendipity rather than rational hair drug design. Thus, to develop more precise therapies for alopecia, the mechanisms of hair growth-promoting effects as well as new drugs and natural hair growth enhancers require exploration.

In previous research, rice bran supercritical CO₂ extract (RB-SCE) was found to be a potent inducer of hair growth in mice11 via 5-alpha-reductase inhibition.12 In addition, the toxicological safety of RB-SCE was investigated using the 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay in RAW264.7 cells. Further safety evaluations included single oral dose toxicity in rats,13 an acute dermal and ocular irritation test,14 a single dose and 4-week repeated dose dermal toxicity study,15 and a genotoxicity assessment.16 Thus, RB-SCE is thought to be safe. Despite its therapeutic potential and safety, no reports have described a clinical study of RB-SCE for alopecia.

Therefore, in the present study, we evaluated the safety of RB-SCE and its effects on markers of hair growth in alopecia. We expect that the results of this open-label trial can provide basic clinical information regarding changes in biochemical markers after RB-SCE treatment.

MATERIALS AND METHODS

Test Material RB-SCE (rice bran, Oryza sativa L. var. japonica) was prepared in a semi-continuous flow-type apparatus with a 3-L extractor.11 Test tonic products with or without RB-SCE were prepared and kindly supplied by Kolmar Korea (Sinjeong-ri, Yeongi-gun, Chungcheongnam-do, Korea). The studied formulations (Table 1) were prepared.
in a PRIMIX RM homomixer (PRIMIX Co., Ltd., Japan) at 3000 rpm within 10 min and supplemented with 0.5% (w/w) RB-SCE. A placebo formulation was prepared without RB-SCE.

Study Design  The study design and a flow chart of study subjects are shown in Fig. 1. We enrolled 50 patients who were diagnosed with alopecia according to the criteria for the diagnosis of alopecia in Korean patients. Informed consent was obtained from all study participants. To assess the degree of hair loss, we used the Hamilton–Norwood classification for men and the Ludwig classification for women. This was a double-blind randomized controlled clinical trial. The patient group comprised a total of 50 subjects including 22 women and 28 men. They were enrolled in either the RB-SCE group or the placebo group by the table of random numbers. They were randomized 1:1 to either RB-SCE or placebo treatment (25 patients each; Table 2). The RB-SCE group received a dermal application of a test tonic product containing 0.5% RB-SCE to bald scalp skin and the placebo group received a dermal application of a test tonic product that contained no RB-SCE. At the baseline visit, subjects were given a plastic bottle containing a 16-week supply of their assigned test tonic (with or without RB-SCE). They were instructed to treat the scalp with 4 mL of solution once or twice a day at approximately 12-h intervals (total daily dose of 8 mL).

Scalp photography and phototrichography (Folliscope 2.5; LeadM Co., Seoul, Korea) were performed at baseline (0 week) and after 8 and 16 weeks of treatment. The study protocol was approved by the institutional review board (IRB) of the Korea University Ansan Hospital (IRB No. AS13141). All procedures were conducted in accordance with the ethics standards of the Declaration of Helsinki and Good Clinical Practice Guidelines.

To ensure compliance and monitor adverse effects, subjects underwent diagnostic tests conducted by a dermatologist after 8 and 16 weeks. To assess treatment compliance, subjects were asked to bring in their solution bottle at the end of the study and the remaining test tonic volume was measured by research staff. Restricted food and drugs during the study period included any hair growth-promoting agents, alopecia treatments, prostatic disease treatments, hormone products, and skin and hair health supplements.

For all site visits, subjects were asked to visit at the same time in the morning. Physical examinations including vital sign and hair measurements were performed at baseline and after 8 and 16 weeks. The patient questionnaire assessment and skin tolerance and safety evaluations by clinical observation were also performed after 8 and 16 weeks of treatment.

Inclusion Criteria  The study inclusion criteria were as follows: age greater than 18 years; a diagnosis of alopecia more than 2 weeks prior to the study; treatment requirement; and agreement to participate in this clinical trial after receipt of an explanation of the objectives, methods, and efficacy of the study drug.

Table 1. Formulation of the Test Tonic Product Containing RB-SCE

| INCI         | Percentage of components (w/w) |
|-------------|-------------------------------|
| Water (aqua), demineralized | as 100% |
| Glycerin    | 1.0                           |
| Hydroxyethyl cellulose | 0.5            |
| Tetrasodium EDTA | 0.03                      |
| C12–14 Pareth-12 | 2.0                        |
| Hyaluronic acid   | 0.5                         |
| Alcohol      | 15.0                         |
| RB-SCE       | 0.5                          |
| PEG-40 castor oil | 2.0                      |
| Triethanolmine | 0.3                      |

INCI=International Nomenclature of Cosmetic Ingredients; RB-SCE=rice bran supercritical CO2 extract.

Table 2. Age and Sex Distribution of Alopecia Areata Patients

| Enrollment | Completion |
|------------|------------|
| N          | Age (years) | N          | Age (years) |
|------------|-------------|------------|-------------|
| RB-SCE treated group |
| Male       | 12          | 39.0±8.6  | 9           | 41.0±9.2  |
| Female     | 13          | 42.6±12.8 | 12          | 42.2±13.3 |
| Sub-total  | 25          | —         | 21          | —         |
| Mean       | —           | 40.1±11.0 | —           | 41.7±11.5 |
| Placebo group |
| Male       | 16          | 41.9±8.2  | 13          | 41.3±6.6  |
| Female     | 9           | 50.0±15.7 | 9           | 50.0±15.7 |
| Sub-total  | 25          | —         | 22          | —         |
| Mean       | —           | 44.8±11.9 | —           | 44.9±11.8 |
| Sum (male/female) |
| Total      | 50 (28/22)  | —         | 43 (22/21)  | —         |
| Range      | 25–68       | —         | 28–68       | —         |
| Mean       | 42.0±11.37  | —         | 43.3±11.58  | —         |

RB-SCE=Test tonic containing RB-SCE; Placebo=Test tonic with no RB-SCE. The patient group comprised a total of 50 subjects including 22 women and 28 men. Of these, 43 subjects (12 men and 11 women) completed the study visits and intervention. Six men and one woman were excluded from the efficacy analysis due to poor compliance (<80%).
Exclusion Criteria  The study exclusion criteria were as follows: treatment with other products or medications within 2 weeks before study initiation; allergy to any component of RB-SCE; medication for another disease; pregnancy or breastfeeding; enrollment in another clinical study within 3 months of this study; inability to understand the objectives and methods of this clinical trial; and inappropriateness for study participation as deemed by the clinician.

Phototrichography  Hair measurement was performed via phototrichography according to the methods of Oh and Son(17) using a computerized hand-held USB camera (Folliscope 2.5) at baseline and after 8 and 16 weeks. Briefly, the primary site of scalp baldness was tattooed and examined for hair density (number of hairs per square centimeter) and hair diameter (micrometer). Hair density per square centimeter was determined manually under 50-fold magnification. Hair diameter was measured under 100-fold magnification.

Expert Panel Assessment of Global Photographs  Standardized global photographs of the primary site of scalp baldness were obtained at baseline, 8 weeks, and 16 weeks. The patient’s head was placed in a stereotactic device to maintain consistency of patient positioning and photographic distance.(19) Subjects were instructed to maintain their hairstyle throughout the study and to avoid dying their hair or using any hair enhancement procedures.

Global photographs were reviewed in a blinded manner by an expert panel of three dermatologists (Jae Beom Park, Sung Kyu Jung, and Sang Wook Son) at the end of the trial using a 7-point scale.(19) Assessments included the percentage of scalp affected by alopecia and a scoring of hair regrowth from −3 to +3 using a 7-point scale as follows: greatly, moderately, or slightly decreased; no change; slightly, moderately, or greatly increased.

Patient Questionnaire Assessment  After 8 and 16 weeks of treatment, each subject was asked to perform a self-assessment of personal hair growth and scalp appearance. The self-assessment questionnaire parameters included size of the vertex spot, hair loss on top of the scalp, bitemporal recession, hair shedding, hair quality, and overall satisfaction.(20) Patient satisfaction was assessed using the 3-point rating scale (improved, no change, or worse) most commonly used in alopecia-related research.(17)

Skin Tolerance and Safety Evaluations  Product safety was assessed by a dermatologist’s clinical observation as well as subject feedback. Adverse effects were recorded using WHO Adverse Reaction Terminology and evaluated for a causal relationship to the treatment. The objective signs were erythema, edema, scaling, and papule. The subjective signs included itching, prickling, burning, stinging, stiffness, tightness, burning of the eyes, weeping, etc. The frequency, duration, and intensity of each symptom and a possible or probable relationship with the test samples were investigated.

Statistical Analysis  All statistical analyses were performed using SPSS software (version 12.0; SPSS Inc., Chicago, IL, U.S.A.). A paired t-test was used to evaluate statistically significant differences in hair density, hair diameter, and expert panel assessment. Student’s t-test was used to evaluate increases in hair density and hair diameter. The chi-square test was used to evaluate statistically significant between-group differences in the questionnaire analysis. Statistical significance was accepted at p-values less than 0.05.

RESULTS  

Characterization of Patients  This study took place between February 2014 and July 2014. Of the 61 people who were screened for study inclusion, 50 subjects (28 men and 22 women) participated. Seven subjects (6 men and 1 woman) withdrew after the baseline visit for personal reasons, and 43 subjects (22 men and 21 women) completed the study (Table 2). Patient ages ranged from 28 to 68 years (mean, 43.3±11.6 years). Mean ages were 41.7 years in the RB-SCE group and 44.9 years in the placebo group.

Hair Density  At baseline, the average number of hairs in male subjects in the RB-SCE group was 93.50 strands/cm². After RB-SCE treatment, hair density increased to 96.56 and 103.22 strands/cm² at 8 and 16 weeks, respectively. The hair density of the RB-SCE group was not significantly increased after 8 weeks but was significantly increased after 16 weeks. In the placebo group, hair density increased from 88.19 strands/cm² at baseline to 88.00 and 90.89 strands/cm² at 8 and 16 weeks, respectively. The hair density of the placebo group was not significantly increased after 8 and 16 weeks (Table 3). The average increase in the number of hairs was 3.06 and 9.72 strands/cm² in the RB-SCE group and only −0.19 and 2.69 strands/cm² in the placebo group at 8 and 16 weeks, respectively. The increase in hair density did not significantly differ between the RB-SCE and placebo groups at 8 weeks but did significantly differ at 16 weeks (Table 3, p=0.410 and p=0.034).

In female subjects, the average number of hairs in the RB-SCE group was 81.96 strands/cm² at baseline. After RB-SCE treatment, hair density significantly increased to 89.38 and 95.59 strands/cm² at 8 and 16 weeks, respectively. In the pla-

Table 3. Hair Density at 0, 8 and 16 Weeks after Treatment in Male and Female Subjects

|                      | Hair density (strand/cm²) | Pairwise comparison p value | Changes of hair density (strand/cm²) |
|----------------------|---------------------------|-----------------------------|-------------------------------------|
|                      | 0wk | 8wk | 16wk | 0wk vs. 8wk | 8wk vs. 16wk | 0wk vs. 16wk | ΔX1 | ΔX2 | ΔX3 |
| **Male**             |     |     |      |              |                |                |     |     |     |
| RB-SCE               | 93.50±11.8 | 96.56±11.2 | 103.22±10.1 | 0.106 | 0.000 | 0.000 | 3.06±5.04 | 6.67±3.35 | 9.72±4.62 |
| Placebo              | 88.19±23.4 | 88.00±14.8 | 90.89±17.5 | 0.949 | 0.055 | 0.269 | −0.19±10.7 | 2.89±4.90 | 2.69±8.37 |
| p                    |     |     |      | 0.410 | 0.059 | 0.034 |                |                |                |
| **Female**           |     |     |      |              |                |                |     |     |     |
| RB-SCE               | 81.96±13.6 | 89.38±8.4 | 95.59±8.4 | 0.024 | 0.005 | 0.006 | 7.42±9.82 | 6.21±6.10 | 13.63±13.87 |
| Placebo              | 70.56±11.1 | 76.67±7.3 | 80.94±10.0 | 0.089 | 0.126 | 0.039 | 6.11±9.47 | 4.28±7.51 | 10.39±12.66 |
| p                    |     |     |      | 0.280 | 0.148 | 0.198 |                |                |                |

RB-SCE=Test tonic with RB-SCE; Placebo=Test tonic without RB-SCE. ΔX1=hair density after 8 wk−hair density at 0 wk; ΔX2=hair density after 16 wk−hair density after 8 wk; ΔX3=hair diameter after 16 wk−hair diameter at 0 wk.
cebo group, hair density increased from 70.56 strands/cm² at baseline to 76.67 and 80.94 strands/cm² at 8 and 16 weeks, respectively. The hair density of the placebo group was not significantly increased after 8 weeks but was significantly increased after 16 weeks (Table 3). The average increase in the number of hairs was 7.42 and 13.63 strands/cm² in the RB-SCE group and only 6.11 and 10.39 strands/cm² in the placebo group at 8 and 16 weeks, respectively. The increase in hair density did not significantly differ between the RB-SCE and placebo groups at 8 and 16 weeks (respectively). The hair density of the placebo group was not significantly increased at 16 weeks (vs. baseline to 76.67 and 80.94 strands/cm² at 8 and 16 weeks, respectively. In the placebo group, hair density did not significantly differ between the RB-SCE and placebo groups at 8 and 16 weeks, respectively.

**Hair Diameter**

The average hair diameter in male subjects in the RB-SCE group was 57µm at baseline, increasing to 66 and 75µm after 8 and 16 weeks of treatment, respectively. In the RB-SCE group, hair diameter was significantly increased after 8 and 16 weeks. In the placebo group, hair diameter increased from 62µm at baseline to 73 and 74µm after 8 and 16 weeks, respectively. In the placebo group, hair diameter did not significantly increase after 8 weeks but was significantly increased at 16 weeks (Table 4). The change in diameter did not differ significantly between the RB-SCE and placebo groups at 8 weeks (8.6 vs. 11.0, p=0.586), and the change from baseline to 16 weeks in the RB-SCE group was 1.4-fold higher (16.6 vs. 11.5, p=0.389) (Table 4).

**Expert Panel Assessment of Global Photographs**

Global photographs were reviewed in a blinded manner by expert panels composed of three dermatologists using a 7-point scale (Fig. 2). After 16 weeks of treatment, the experts observed improved hair growth in the RB-SCE group (score=0.89±0.601, p=0.002), while no improvement in hair growth was observed in male subjects in the placebo group (0.08±0.862, p=0.753). At 8 weeks of treatment, the average score was 0.67 in the RB-SCE group and 0.00 in the placebo group, and the difference was not statistically significant (p=0.608). However, at 16 weeks of treatment, the average score in the RB-SCE group (0.89±0.601) was clearly higher than that in the placebo group (0.08±0.862) (p=0.024) (Table 5).

After 16 weeks of treatment, the experts observed improved hair growth in female subjects in both the RB-SCE group (score=1.25±0.452, p=0.000) and the placebo group (1.11±0.601, p=0.013). At 8 weeks of treatment, the average score was 0.67 in the RB-SCE group and 0.56 in the placebo group, and the difference was not statistically significant (p=0.717). At 16 weeks of treatment, the average score in the RB-SCE group (1.25±0.452) and in the placebo group

### Table 4. Hair Diameter at Baseline and 8 and 16 Weeks after Treatment in Male and Female Subjects

|                  | Hair diameter (µm) | Increase of hair diameter (µm) |
|------------------|-------------------|-------------------------------|
|                  | 0 wk  | 8 wk  | 16 wk | 0 wk vs. 8 wk | 8 wk vs. 16 wk | 0 wk vs. 16 wk | ΔX1   | ΔX2   | ΔX3   |
| Male             |       |       |       |               |               |               |       |       |       |
| RB-SCE           | 57±18  | 66±14 | 75±16 | 0.013         | 0.000          | 0.001         | 8.6±8.1 | 8.8±3.6 | 17.3±10.2 |
| Placebo          | 59±17  | 66±16 | 69±16 | 0.059         | 0.012          | 0.011         | 6.8±11.8 | 2.8±3.5 | 9.7±11.6 |
| Female           |       |       |       |               |               |               |       |       |       |
| RB-SCE           | 72±15  | 80±11 | 89±14 | 0.027         | 0.001          | 0.001         | 8.0±10.9 | 8.6±6.8 | 16.6±13.3 |
| Placebo          | 62±14  | 73±10 | 74±11 | 0.046         | 0.672          | 0.027         | 11.0±13.9 | 0.5±3.4 | 11.5±12.8 |

RB-SCE = Test tonic with RB-SCE; Placebo = Test tonic without RB-SCE. ΔX1 = hair diameter after 8 wk – hair diameter at 0 wk; ΔX2 = hair diameter after 16 wk – hair diameter after 8 wk; ΔX3 = hair diameter after 16 wk – hair diameter at 0 wk.
(1.11±0.601) and the difference were not statistically significant (p=0.552) (Table 5).

**DISCUSSION**

Alopecia is a common form of hair loss in both men and women, affecting approximately 0.2 to 2% of the world’s population. Although topical minoxidil and oral finasteride are available for the treatment of alopecia, these medicines have sometimes been reported to have adverse effects. In our previous study, RB-SCE showed hair growth-promoting potential similar to that of 3% minoxidil, as evidenced by findings of hair follicles induced in the anagen stage, and a significant increase in the number of hair follicles in C57BL/6 mice. However, there have been no clinical studies of RB-SCE. We therefore performed this clinical study to confirm the ability of RB-SCE to improve hair loss in 43 patients treated with or without RB-SCE.

Clinical research on topical alopecia treatments included clinical studies of procyanidin B-2 and minoxidil. After 48 weeks of male pattern hair loss treatment, the parameter known as non-vellus hair count (mean change from baseline) in the 5% minoxidil, 2% minoxidil, and placebo groups measured 18.6, 12.7, and 3.9 strands/cm², respectively. The change from baseline in the non-vellus hair count was significantly superior with 5% topical minoxidil compared to...
2% topical minoxidil and placebo. After 48 weeks of female pattern hair loss treatment, the non-vellus hair count (mean change from baseline) in the 5% minoxidil, 2% minoxidil, and placebo groups measured 24.5, 20.7, and 9.4 strands/cm², respectively.23) As in the male patients, 5% topical minoxidil was significantly superior to 2% topical minoxidil and placebo in the female patients. To investigate the effects of topical procyanidin B-2 (1%), which is purified from apples, on the scalp and hair, a placebo controlled clinical trial was performed with RB-SCE and placebo, respectively, showing a statistically significant increase (p=0.001; Table 4). The hair diameter (mean change from week 8) after 16 weeks was 8.6 µm (from 80 to 89 µm) and 0.5 µm (from 73 to 74 µm) in female subjects with RB-SCE and placebo, respectively, showing a significant increase (p=0.004; Table 5). The increase in hair diameter in the RB-SCE group after 16 weeks (17.3 and 16.6 µm in male and female subjects, respectively) was higher than that reported for 1% procyanidin B-2 after 16 weeks (8.04 µm).

Regarding the expert panel assessment of global photographs in male subjects, at 16 weeks of treatment, the average score in the RB-SCE group (0.89±0.601) was clearly higher than that in the placebo group (0.08±0.862), and the difference was statistically significant (p=0.024) (Table 5). In female subjects at 16 weeks of treatment, the average score in the RB-SCE group (1.25±0.452) and in the placebo group (1.11±0.601) and the difference were not statistically significant (p=0.552) (Table 5).

Self-questionnaires have been reported useful for the evaluation of new potential hair growth-promoting candidates or medicines.4,17,23) In the study of Olsen et al. in male patients,4) patient questionnaire hair growth composite scores at week 48 (efficacy-evaluable population) for 5% minoxidil, 2% minoxidil, and placebo were 60.4, 56.8, and 50.7, respectively. In the study of Lucky et al. in female patients,23) patient questionnaire hair growth composite scores at week 48 (efficacy-evaluable population) for 5% minoxidil, 2% minoxidil, and placebo were 64.5, 60.5, and 56.4, respectively. In our study, the population with improvement in bitemporal recession and hair shedding in the RB-SCE group of male subjects was signifi-

### Table 7. Questionnaire Analysis Results in Female Subjects

|                          | RB-SCE (%) | Placebo (%) | p Value |
|--------------------------|------------|-------------|---------|
|                          | 8 wk/16 wk | 8 wk/16 wk  |         |
| Size of vertex spot      |            |             |         |
| Improved                 | 33.3       | 33.3        | 1       |
| No change                | 66.7       | 66.7        | 0.604   |
| Worse                    | 0.0        | 0.0         |         |
| Hair loss on top of scalp|            |             |         |
| Improved                 | 41.7       | 33.3        | 0.673   |
| No change                | 58.3       | 66.7        | 0.130   |
| Worse                    | 0.0        | 0.0         |         |
| Bitemporal recession     |            |             |         |
| Improved                 | 25.0       | 16.7        | 0.615   |
| No change                | 75.0       | 83.3        | 0.163   |
| Worse                    | 0.0        | 0.0         |         |
| Hair shedding            |            |             |         |
| Improved                 | 41.7       | 58.3        | 0.693   |
| No change                | 50.0       | 33.3        |         |
| Worse                    | 8.3        | 8.3         |         |
| Hair quality             |            |             |         |
| Improved                 | 25.0       | 58.3        | 0.098   |
| No change                | 75.0       | 41.7        | 0.899   |
| Worse                    | 0.0        | 0.0         |         |
| Overall satisfaction     |            |             |         |
| Improved                 | 50.0       | 83.3        | 0.083   |
| No change                | 50.0       | 16.7        | 0.375   |
| Worse                    | 0.0        | 0.0         |         |

The chi-square test was used to evaluate statistically significant between-group differences in the questionnaire analysis. RB-SCE=Test tonic with RB-SCE; Placebo=Test tonic without RB-SCE. —: not determined.
The significant differences in hair density, hair diameter, and expert panel assessment of global photographs were shown in male subjects after 16 weeks of treatment with RB-SCE. In addition, the significant differences between the RB-SCE and placebo groups after 16 weeks showed in hair density, expert panel assessment of global photographs, and questionnaire analysis in male subjects. In female subjects after 16 weeks of treatment with RB-SCE, the significant differences in hair density, hair diameter, and expert panel assessment of global photographs were shown but not significantly different from those of the placebo group.

In a previous study, to examine the hair growth-promoting activity of RB-SCE, we selected linoleic acid (LA), oryzanol (OZ), policosanol (PS), and tocotrienol (TT) as the main components of RB-SCE. In particular, the unsaturated fatty acids such as γ-LA, LA, and oleic acid as well as RB-SCE have been shown to have anti-hair loss activity by inhibiting the 5α-reductase enzyme in androgen-responsive organs. In this study, RB-SCE had a significant hair growth-promoting effect in male subjects but not in female subjects, meaning that RB-SCE may have an effect in androgen-dependent hair loss. Recently, female patients with alopecia were reported to be divided by androgen-dependent female pattern hair loss (FPHL) and androgen-independent FPHL according to the serum androgen levels of the female patients. The analyses of blood chemistry tests including hormonal levels for female patients are needed in further study.

Previous researchers have confirmed the toxicological safety of RB-SCE in RAW264.7 cells. Additional safety evaluations included single oral dose toxicity in rats, an acute dermal and ocular irritation test, a single dose and 4-week repeated dose dermal toxicity study, and a genotoxicity assessment. As urinalysis, hematological tests, clinical biochemistry tests, necropsies, and histopathological examinations were performed in male and female rats after 4-week repeated-dose dorsal administration of RB-SCE, no liver or kidney damage was observed. In addition, in this study, no specific side effects such as irritant contact dermatitis, allergic contact dermatitis, itching, prickling, burning, erythema, oozing, vesicles, skin rashes, and so on were observed in patients receiving RB-SCE. Therefore, RB-SCE is thought to be safe for topical application in humans.

However, the limitations of this study are the single-center study design, small number of subjects, and lack of blood chemistry research including hormonal levels, extensive interviews with patients about hormonal effects detected by sexual dysfunction (e.g., loss of libido), and confirmation of the absence of liver or kidney damage. Further studies, including multicenter studies with longer treatment periods, larger sample-size patient populations, blood chemistry research, and extensive patient interviews, are needed to confirm the present results.

RB-SCE is a mixture of fatty acids and oily materials and not a purified compound. Nevertheless, the increase in hair density and diameter as well as patient satisfaction with 0.5% RB-SCE after 16 weeks were similar to or slightly lower than those reported for 2% minoxidil after 48 weeks or 1% procyandin B-2 after 16 weeks. Therefore, RB-SCE appears to have considerable hair growth-promoting potential.

CONCLUSION

In conclusion, these results suggest that treatment with RB-SCE can improve hair regrowth in human androgen-dependent alopecia without side effects at a moderate dose. Therefore, RB-SCE is a potentially promising source of functional cosmetics and pharmaceuticals developed to treat male pattern and androgen-dependent female pattern hair loss.

Acknowledgment This work was supported by a Grant (No. 311014-03) from the Ministry for Food, Agriculture, Forestry and Fisheries, Republic of Korea.

Conflict of Interest The authors declare no conflict of interest.

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