



Do Kimchi and *Cheonggukjang* Probiotics as a Functional Food Improve Androgenetic Alopecia? A Clinical Pilot Study

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Purpose: Probiotic supplementation demonstrates beneficial effects on serum lipid profiles. We hypothesized that probiotics could benefit patients presenting with alopecia, secondary to improved blood flow to the scalp.

Materials and Methods: Our study included men with stage II to V patterns of hair loss based on the Hamilton–Norwood classification and women with stage I to III patterns of hair loss based on the Ludwig classification. All patients were administered 80 mL of Mogut[®] (a kimchi and *cheonggukjang* probiotic product) twice a day. Hair growth and numbers were measured using the Triple Scope System[®] (KC Technology, Korea) at baseline and after 1 and 4 months of administration of a kimchi and *cheonggukjang* probiotic product.

Results: At baseline, the mean hair count was 85.98±20.54 hairs/cm² and the mean thickness was 0.062±0.011 mm in all patients (n=46). Hair count and thickness had significantly increased at 1 month (90.28±16.13 hairs/cm² and 0.068±0.008 mm, respectively) and at 4 months (91.54±16.29 hairs/cm² and 0.066±0.009 mm, respectively). In this study, we found that a kimchi and *cheonggukjang* probiotic product could promote hair growth and reverse hair loss without associated adverse effects such as diarrhea.

Conclusions: We suggest that the observed improvements in hair count and thickness resulted from initiation of the anagen phase in hair follicles in response to probiotics.

Keywords: Alopecia; Functional food; Leuconostoc; Probiotics; Scalp; Soybeans

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INTRODUCTION

Humans are usually born with approximately 5 million hair follicles, and no new follicles are added after birth [1]. The hair follicle cycle, which begins in utero, comprises 3 stages: the anagen, telogen, and catagen

phases. Anagen represents the growth phase associated with extensive mitotic activity, and 90% to 95% of all hair exists in the anagen phase at any given point in time. Hair then involutes during the catagen phase through apoptosis of the follicular keratinocytes and is converted to club hair. Telogen is the resting phase

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associated with inactivity of the hair follicle. The club hair is shed and new anagen hair growth begins, resuming the cycle [2-4].

Usually, approximately 50 to 100 hairs are shed per day. Hair loss >100 hairs/d is defined as alopecia. There are different types of alopecia that can cause hair loss on the scalp or on other areas of the body [5]. Hair loss can be attributed to multiple factors, including dandruff, hormonal deficiencies, dietary or nutrient deficiencies, certain diseases, chemotherapy, and/or psychological issues, such as stress and depression [6]. In most men, androgenetic alopecia develops with a distinctive “patterned” hair line recession. In women, the presentation may be less clear; typically women will develop a diffuse thinning over the top of the scalp, yielding a “Christmas tree” pattern with more thinning towards the front, although the frontal hairline is maintained [7]. Occasionally, men may develop a female presentation of hair loss and women, primarily those experiencing excess androgen activity, may develop a more men-like hair loss pattern [8]. Five- α reductase inhibitors are used to treat androgenetic alopecia, and are effective for preventing hair loss progression and induction of hair regrowth in androgenetic alopecia in men. However, they are not recommended for women, and side effects, such as erectile dysfunction and decreased libido have been reported [9,10]. Additionally, alopecia may result from sun exposure, consumption of junk food, use of styling tools, and/or extreme weight loss [11]. Alopecia is associated with significant psychosocial consequences and can affect patients’ lives and social behavior, often triggering psychological problems [12]. No robust evidence supports the consistent efficacy of topical treatments, including topical corticosteroids, tacrolimus, cryotherapy, minoxidil, anthralin, or ultraviolet light A combined with oral psoralens in treating alopecia [13], and those options are usually not suitable for patients presenting with extensive alopecia because of their minimal efficacy [14,15]. Minoxidil is a topical vasodilator that prolongs the anagen phase and increases the size of smaller hair follicles [1]. Its exact mechanism of action has not yet been determined, although a few research studies have presented data suggesting that an improved nutritional supply to the scalp secondary to vasodilation may play a key role in its demonstrated efficacy [16,17]. Despite positive effects on alopecia, several adverse effects of commercial hair restorers have been reported, limiting their use for

treatment of patients with alopecia [18,19].

Recently, several experimental and clinical studies have reported that probiotic supplementation demonstrated beneficial effects on serum lipid profiles, indicating improvements in peripheral blood flow [20,21]. Based on these research data, we hypothesized that dietary supplementation of probiotics could benefit patients presenting with alopecia secondary to improved blood flow to the scalp. We investigated the effect of administration of a kimchi and *cheonggukjang* probiotic product on patients with hair loss. Kimchi and *cheonggukjang* (a Korean traditional fermented soybean product) are traditional Korean foods, but ensuring optimal intake of probiotics from kimchi and *cheonggukjang* is difficult, for two main reasons. First, the amount of probiotics varies depending on the ripening period of kimchi, as different ripening periods lead to differences in pH that could affect personal appetite. Koreans consume *cheonggukjang* as a boiled hot soup, so it contains no live probiotics. Thus, administration of live probiotics from kimchi and *cheonggukjang* as a drinkable yogurt would be a more efficient way to obtain the beneficial effects of kimchi and *cheonggukjang*. The primary ingredients in this product are the probiotic-rich kimchi and *cheonggukjang*. All patients were administered a kimchi and *cheonggukjang* probiotic product over the course of 4 months, and hair thickness and count were measured at 1 and 4 months.

MATERIALS AND METHODS

1. Study population

Patients were enrolled in the study between January 2017 and June 2017. Men aged 46.52 ± 10.14 (standard deviation, SD) years showing stage II to V patterns of hair loss based on the Hamilton–Norwood classification and women aged 44.17 ± 10.20 years showing stage I to III patterns of hair loss based on the Ludwig classification were included in this study [22]. The exclusion criteria were: use of any topical medication (such as minoxidil or other solutions for hair growth), intake of oral medication (finasteride, dutasteride, or anti-androgens), laser therapy or chemotherapy within 12 months prior to enrollment in the study, smoking, a history of hair transplantation, pregnant or lactating women, and any chronic active scalp condition other than alopecia. According to a rule of thumb, the sample size was determined to be 23 for each sex [23].

2. Ethics statement

The present study protocol was reviewed and approved by the Institutional Review Board of Cheil General Hospital (Reg. No. CGH-IRB-2016-57). Informed consent was provided by all subjects when they were enrolled.

3. Study design and intervention

All patients were administered 80 mL of a kimchi and *cheonggukjang* probiotic product (Mogut[®]; Coenbio, Seongnam, Korea) twice a day (before breakfast and bedtime). The ingredients of the kimchi and *cheonggukjang* probiotic product were: culture medium with fermented bacilli of kimchi and *cheonggukjang* (*Leuconostoc holzapfelii*, *Leuconostoc mesenteroides*, and *Lactobacillus sakei*; 99.7%), persimmon vinegar (0.1%), Hasuo extract (*Pleuropterus multiflorus*; 0.1%), and extract of Korean black soybean (*Rhynchosia volubilis* Lour; 0.1%).

4. Efficacy evaluation

Hair growth and numbers were measured using the Triple Scope System[®] (KC Technology, Seoul, Korea) after 0 (baseline), 1, and 4 months of administration of the kimchi and *cheonggukjang* probiotic product. All patients were instructed to wash their hair before visiting the hospital and strictly advised against use of hair treatment using cosmetics such as styling gels. The analysis was performed on the top of the patient's head, and the scalp was tattooed to identify the areas for the next measurement. The hair density (number of hairs/cm²) was measured at 5 different sites using a scope at ×60 magnification, and hair thickness (mm) was measured in 5 individual hair strands using a scope at ×100 magnification.

5. Statistical analysis

The Student t-test was used to assess the statistical

significance of differences. All statistical analyses were performed using SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). A p<0.05 was considered to indicate statistical significance. Data are presented as mean±SD.

RESULTS

Forty-six patients were enrolled in this study. All patients completed the study. The patients' characteristics are shown in Table 1. The hair parameters measured after 1 and 4 months of administration of a kimchi and *cheonggukjang* probiotic product were compared with the baseline (0-month) values. At baseline, in all patients (n=46), the hair count was 85.98±20.54 hairs/cm² and thickness was 0.062±0.011 mm. As shown in Table 2, hair count and thickness had significantly increased at 1 month (90.28±16.13 hairs/cm² and 0.068±0.008 mm, respectively) and at 4 months (91.54±16.29 hairs/cm² and 0.066±0.009 mm, respectively) compared to the baseline value (p<0.001). We observed that after 1 month of administration of the kimchi and *cheonggukjang* probiotic product, 63.0% of the total patients (n=29) showed improvements in the measured hair parameters (thickness and count), and 21.8% (n=10) and 4.3% (n=2) of all patients showed improvements in only hair thickness and count, respectively. In 10.9% (n=5) of the total patients, no improvement was observed in either hair parameter that was assessed (Fig. 1). After 4 months, 54.3% (n=25) of all patients showed improvement in both assessed parameters, while 21.8% (n=10) and 17.4% (n=8) of the total patients showed improved hair thickness and count, respectively, and 6.5% (n=3) of the total patients showed no improvement in either assessed parameter (Fig. 2).

We analyzed data based on sex (23 male and 23 female) to determine whether the efficacy of the kimchi and *cheonggukjang* probiotic product differed by sex. In male patients, hair count increased steadily from baseline to 4 months (86.91±22.21 hairs/cm² at the initial visit, 88.17±17.50 hairs/cm² at 1 month, and

Table 1. Characteristics of the study patients with alopecia

Characteristic	Male patients (n=23)	Female patients (n=23)
Age (y)	46.52±10.14	44.17±10.20
Past history of alopecia treatment	None	None
Menopause (%)	N/A	52.1

Values are presented as mean±standard deviation or percent only. N/A: not available.

Table 2. Results of hair parameters in all patients

Variable	Initial (n=46)	1 month (n=46)	4 months (n=46)	p-value
Counts (/cm ²)	85.98±20.54	90.28±16.13	91.54±16.29	<0.001
Thickness (mm)	0.062±0.011	0.068±0.008	0.066±0.009	<0.001

Values are presented as mean±standard deviation.

90.78±17.65 hairs/cm² at 4 months; p<0.001). Thickness had also increased at 1 month (0.064±0.007 mm) and 4 months (0.063±0.006 mm) compared to baseline (0.058±0.009 mm, p=0.002) (Table 3). In female patients,

hair count had increased at 1 month (92.39±14.72 hairs/cm²) and 4 months (92.30±15.17 hairs/cm²) compared to the initial visit (85.04±19.18 hairs/cm²) (p<0.001). After 1 and 4 months, hair thickness in female patients was observed to have increased (0.072±0.006 mm and 0.072±0.010 mm, respectively) compared to baseline (0.066±0.011 mm, p=0.001) (Table 4). We observed that 52.2% (n=12) of male and 73.9% (n=17) of female patients showed improvement in both parameters (hair thickness and count) after 1 month of administration of the kimchi and *cheonggukjang* probiotic product. In 39.1% (n=9) of male patients, we observed an improvement in only hair thickness, without any change in hair count during the same period. In 8.7% (n=2) of men, the hair parameters were unaffected following administration of the kimchi and *cheonggukjang* probiotic product over 1 month. After 1 month of probiotic administration, 4.3% (n=1) and 8.7% (n=2) of female pa-

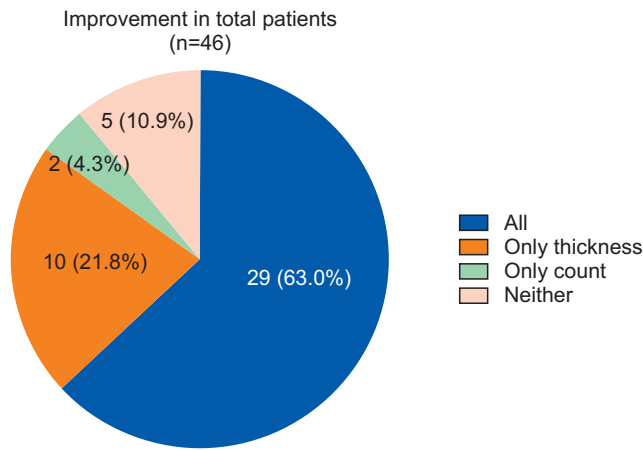


Fig. 1. Results of all patients at 1 month.

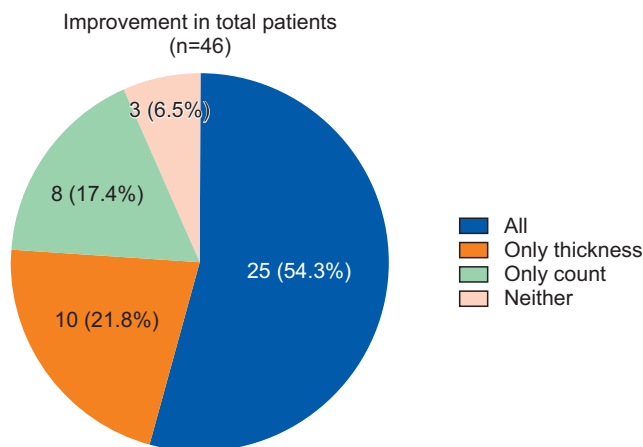


Fig. 2. Results of all patients at 4 months.

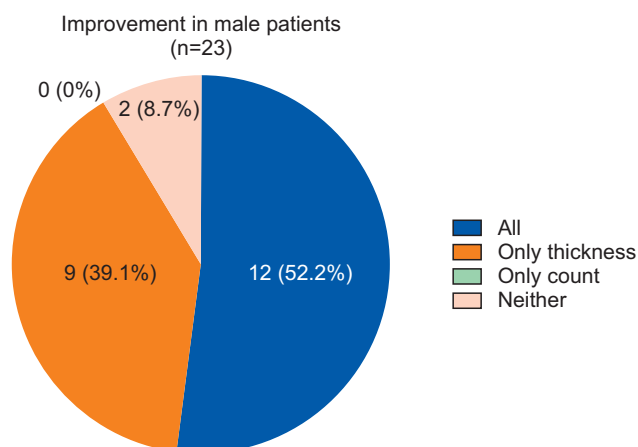


Table 3. Results of hair parameters in male patients

Variable	Initial (n=23)	1 month (n=23)	4 months (n=23)	p-value
Counts (/cm ²)	86.91±22.21	88.17±17.50	90.78±17.65	<0.001
Thickness (mm)	0.058±0.009	0.064±0.007	0.063±0.006	0.002

Values are presented as mean±standard deviation.

Table 4. Results of hair parameters in female patients

Variable	Initial (n=23)	1 month (n=23)	4 months (n=23)	p-value
Counts (/cm ²)	85.04±19.18	92.39±14.72	92.30±15.17	<0.001
Thickness (mm)	0.066±0.011	0.072±0.006	0.072±0.010	0.001

Values are presented as mean±standard deviation.

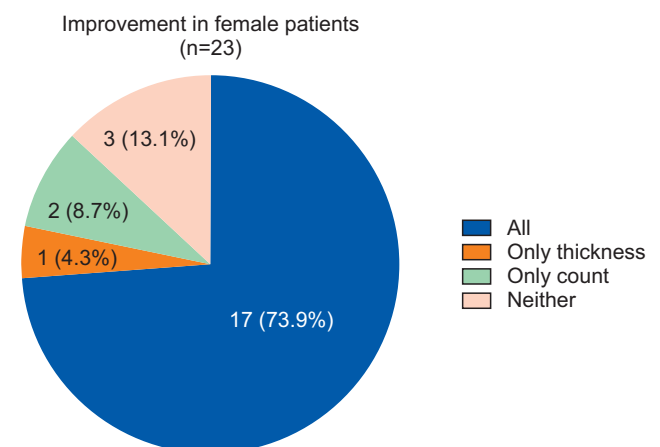


Fig. 3. Results by sex at 1 month.

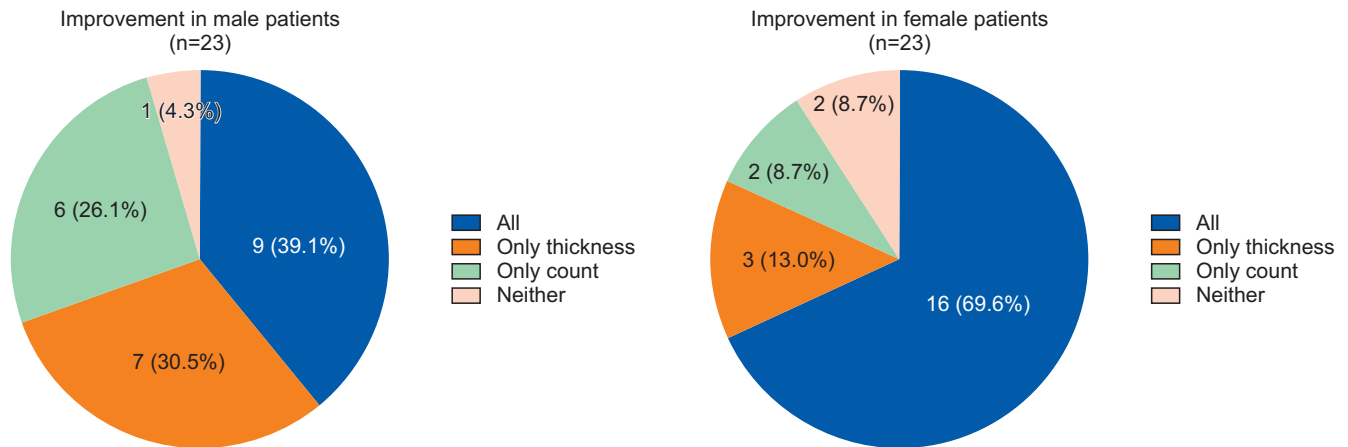


Fig. 4. Results by sex in 4 months.



Fig. 5. Response to administration of a kimchi and *cheonggukjang* probiotic product at baseline (0 month) and 4 months were measured by the Triple Scope System® (×20 magnification).

tients showed improved hair thickness and hair count, respectively. We observed that in 13.1% (n=3) of female patients, both hair parameters were unaffected after 1 month of kimchi and *cheonggukjang* probiotic product administration (Fig. 3). An improvement in both hair parameters was noted after 4 months of probiotic product administration in 39.1% (n=9) of male and 69.6% (n=16) of female patients. Hair thickness had improved in 30.5% (n=7) of male and 13.0% (n=3) of female patients after 4 months of administration of the kimchi and *cheonggukjang* probiotic product. We observed that 26.1% (n=6) of male and 8.7% (n=2) of female patients showed an improved hair count during the same period. No improvement in either hair parameter was observed in 4.3% (n=1) of male and 8.7% (n=2) of female patients after 4 months of probiotic administration (Fig. 4). Fig. 5 presents a vertex view of female and male patients with alopecia showing that administration of the kimchi and *cheonggukjang* probiotic could increase hair density and number after 4 months when compared with baseline (0 month).

DISCUSSION

As their health benefits have become known, probiotics are being widely used globally. Probiotics primarily include bacteria from the genera *Streptococcus*, *Enterococcus*, *Pediococcus*, *Weissella*, and *Lactobacillus*, although the most commonly used probiotics belong to *Lactobacillus* and *Bifidobacterium* spp. [24]. Probiotics are live organisms that are primarily used to improve the signs and symptoms of gastrointestinal disorders such as diarrhea, irritable bowel syndrome, constipation, and lactose intolerance, as well as to inhibit the excessive proliferation of pathogenic intestinal bacteria. However, recent studies have suggested that probiotics could have beneficial effects that extend beyond gastrointestinal health, as they have demonstrated efficacy in improving certain metabolic disorders such as hypertension [25], hypercholesterolemia [21], and atherosclerosis [26]. The suggested mechanisms of probiotic action in metabolic disorders include inhibition of pathogen adhesion to the gut mucosa, stabilization

of microbial flora, and/or improvement of mucosal integrity and barrier function, which can improve energy metabolism and insulin sensitivity [27]. Metabolic diseases such as hypercholesterolemia negatively affect microvascular function, which can be reversed with use of cholestyramine lipid-lowering therapy [28]. Based on these data, intake of appropriate quantities of probiotics could lead to a beneficial effect on peripheral vascular blood flow and hair growth.

The kimchi and *cheonggukjang* probiotic product analyzed in this study included various kinds of probiotics and prebiotics obtained from kimchi, *cheonggukjang*, and natural herbs. Choi et al [5] reported that ultra-high molecular weight poly- γ -glutamic acid (UHMW γ -PGA) isolated from *Bacillus subtilis* (used to ferment *cheonggukjang*) could improve hair growth *in vivo*. The authors showed that UHMW γ -PGA inhibited activity of 5- α reductase, an enzyme produced in the prostate, adrenal glands, and scalp, which metabolizes the male hormone testosterone into dihydrotestosterone [29], resulting in an improvement of alopecia in men. Thus, in that study, we concluded that the difference in the pattern of improvement observed between men and women was secondary to the difference in its effect on the 5- α reductase present in the scalp.

In our present study, all enrolled patients were administered a kimchi and *cheonggukjang* probiotic product over a maximum period of 4 months. Overall, 93% of all patients demonstrated beneficial effects in terms of the hair parameters that were assessed (thickness and hair count); furthermore, the proportion of those who experienced no effects decreased over time (10.9% *vs.* 6.5%) (Fig. 1, 2). These effects were evident within a month of intake of the kimchi and *cheonggukjang* probiotic product. The effectiveness of the kimchi and *cheonggukjang* probiotic product varied between men and women. Men were more likely to experience an effect on only hair thickness (30.4%) or only hair count (26.1%) than an effect on both parameters (39.1%). In contrast, most women showed a positive effect on both hair parameters that were assessed (65.2%), and only 13.0% and 8.7% of women showed improvements in only hair thickness or only hair count, respectively. We observed that administration of the kimchi and *cheonggukjang* probiotic product was ineffective in 4.3% of men and 8.7% of women (Fig. 4). *Cheonggukjang* is a known source of thrombolytic enzymes. Jeong et al [30] studied the characterization of

a fibrinolytic enzyme from *Bacillus subtilis* CH3-5 that was isolated from *cheonggukjang*. This thrombolytic enzyme could increase the peripheral blood flow, including to the scalp, and increase the amount of nutrition provided to hair follicles.

In this study, the efficacy of the kimchi and *cheonggukjang* probiotic product was different between male and female patients, as improvements in both criteria (thickness and count) at 1 month (73.9% *vs.* 52.2%) and 4 months (65.2% and 39.1%) were more common than in male patients in the same period. However, male patients were more likely to experience improvements in only hair thickness at 1 month (39.1% *vs.* 4.3%) and 4 months (30.4% *vs.* 13.0%) than female patients in the same period. The prevalence of androgenetic alopecia in Korean shows a sex bias, as 10.8% of Korean men and 3.8% of Korean women in their 40s are diagnosed with androgenetic alopecia [31]. According to our data, we suggest that kimchi and *cheonggukjang* probiotics exert limited effects on androgenetic alopecia, and further study is therefore needed to verify the different effects of kimchi and *cheonggukjang* probiotics on men and women.

The use of drugs associated with hair regrowth such as finasteride and minoxidil is limited and temporary, due to adverse effects associated with their use, such as irregular heartbeat and weight gain [32]. In this study, we found that a kimchi and *cheonggukjang* probiotic product could promote hair growth and reverse hair loss without associated adverse effects such as diarrhea. Thus, we conclude that the use of natural probiotic products is a safer treatment strategy for patients presenting with alopecia.

This study has some limitations. First, we did not measure changes in the blood flow of the scalp and or blood lipid profiles of all patients enrolled this study. Second, we did not use a placebo group as a negative control. However, we did compare the effects of probiotics before and after administration. Third, the observation period was relatively short, and the number of patients was relatively small; therefore, we were not able to establish whether the probiotic effects on alopecia would be reversed or maintained during a longer period.

CONCLUSIONS

To summarize, we suggest that the observed im-

provements in hair count and thickness resulted from initiation of the anagen phase in hair follicles secondary to the improved blood flow and modulation of androgenetic effects by probiotics. However, ours is a clinical study. Therefore, further studies investigating the mechanism of action of probiotics and their role in hair growth are warranted.

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Conflicts of Interest

Myeong-Seung Shim and Kyu Jin Yum are advisers and Ju Tae Seo is non-executive director of the Coenbio R&D Center, Seongnam, Korea, but they had no influence on this work in relation with the company or its products. The other authors have no potential conflicts of interest to disclose.

Author Contribution

Conceptualization: JTS, HSL. Data curation: HSL. Formal analysis: HSL. Funding acquisition: JTS. Investigation: JTS, HSL. Methodology: JTS. Project administration: JTS, HSL. Resources: JTS. Supervision: KJY, MSS. Validation: JTS, HSL. Visualization: HSL. Writing—original draft: DWP, HSL. Writing—review & editing: DWP, HSL.

Data Sharing Statement

The data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study.

REFERENCES

1. Qi J, Garza LA. An overview of alopecias. *Cold Spring Harb Perspect Med* 2014;4:a013615.
2. Jang SK, Kim ST, Lee DI, Park JS, Jo BR, Park JY, et al. Decoc-tion and fermentation of selected medicinal herbs promote hair regrowth by inducing hair follicle growth in conjunction with Wnts signaling. *Evid Based Complement Alternat Med* 2016;2016:4541580.
3. Kwon OS, Oh JK, Kim MH, Park SH, Pyo HK, Kim KH, et al. Human hair growth ex vivo is correlated with in vivo hair growth: selective categorization of hair follicles for more reliable hair follicle organ culture. *Arch Dermatol Res* 2006;297:367-71.
4. Rile N, Liu Z, Gao L, Qi J, Zhao M, Xie Y, et al. Expression of Vimentin in hair follicle growth cycle of inner Mongolian Cashmere goats. *BMC Genomics* 2018;19:38.
5. Choi JC, Uyama H, Lee CH, Sung MH. In vivo hair growth promotion effects of ultra-high molecular weight poly- γ -glutamic acid from *Bacillus subtilis* (Chungkookjang). *J Microbiol Biotechnol* 2015;25:407-12.
6. Stefanato CM. Histopathology of alopecia: a clinicopathologi-cal approach to diagnosis. *Histopathology* 2010;56:24-38.
7. Shapiro J. Clinical practice. Hair loss in women. *N Engl J Med* 2007;357:1620-30.
8. McElwee KJ, Shapiro JS. Promising therapies for treating and/or preventing androgenic alopecia. *Skin Therapy Lett* 2012;17:1-4.
9. Blumeyer A, Tosti A, Messenger A, Reygagne P, Del Marmol V, Spuls PI, et al.; European Dermatology Forum (EDF). Evi-dence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men. *J Dtsch Dermatol Ges* 2011;9 Suppl 6:S1-57.
10. Gur S, Kadowitz PJ, Hellstrom WJ. Effects of 5-alpha reduc-tase inhibitors on erectile function, sexual desire and ejacula-tion. *Expert Opin Drug Saf* 2013;12:81-90.
11. Gordon KA, Tosti A. Alopecia: evaluation and treatment. *Clin Cosmet Investig Dermatol* 2011;4:101-6.
12. Campo D, Pisani A. Psychogenic alopecia. *G Ital Dermatol Venereol* 2008;143:283-7.
13. Renert-Yuval Y, Guttman-Yassky E. The changing landscape of alopecia areata: the therapeutic paradigm. *Adv Ther* 2017;34:1594-609.
14. Delamere FM, Sladden MM, Dobbins HM, Leonardi-Bee J. Interventions for alopecia areata. *Cochrane Database Syst Rev* 2008;(2):CD004413.
15. Shapiro J. Current treatment of alopecia areata. *J Investig Dermatol Symp Proc* 2013;16:S42-4.
16. Gümüş N, Odemiş Y, Yılmaz S, Tuncer E. Effect of topically applied minoxidil on the survival of rat dorsal skin flap. *Aes-thetic Plast Surg* 2012;36:1382-6.
17. Gupta AK, Charrette A. Topical minoxidil: systematic review and meta-analysis of its efficacy in androgenetic alopecia. *Skinmed* 2015;13:185-9.
18. Hagemann T, Schlütter-Böhmer B, Allam JP, Bieber T, Novak N. Positive lymphocyte transformation test in a patient with allergic contact dermatitis of the scalp after short-term use of topical minoxidil solution. *Contact Dermatitis* 2005;53:53-5.
19. Motofei IG, Rowland DL, Georgescu SR, Tampa M, Paunica S, Constantin VD, et al. Post-finasteride adverse effects in male

- androgenic alopecia: a case report of vitiligo. *Skin Pharmacol Physiol* 2017;30:42-5.
20. Poller WC, Berger A, Dreger H, Morgera S, Enke-Melzer K. Lipoprotein apheresis in patients with peripheral artery disease and lipoprotein(a)-hyperlipoproteinemia: 2-year follow-up of a prospective single center study. *Atheroscler Suppl* 2017;30:174-9.
 21. Shimizu M, Hashiguchi M, Shiga T, Tamura HO, Mochizuki M. Meta-analysis: effects of probiotic supplementation on lipid profiles in normal to mildly hypercholesterolemic individuals. *PLoS One* 2015;10:e0139795.
 22. Bouhanna P. Multifactorial classification of male and female androgenetic alopecia. *Dermatol Surg* 2000;26:555-61.
 23. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. *Pharm Stat* 2005;4:287-91.
 24. Mathipa MG, Thantsha MS. Probiotic engineering: towards development of robust probiotic strains with enhanced functional properties and for targeted control of enteric pathogens. *Gut Pathog* 2017;9:28.
 25. Lye HS, Kuan CY, Ewe JA, Fung WY, Liong MT. The improvement of hypertension by probiotics: effects on cholesterol, diabetes, renin, and phytoestrogens. *Int J Mol Sci* 2009;10:3755-75.
 26. Tsai TY, Chu LH, Lee CL, Pan TM. Atherosclerosis-preventing activity of lactic acid bacteria-fermented milk-soymilk supplemented with *Momordica charantia*. *J Agric Food Chem* 2009;57:2065-71.
 27. Hur KY, Lee MS. Gut microbiota and metabolic disorders. *Diabetes Metab J* 2015;39:198-203.
 28. Abularrage CJ, Sidawy AN, Aidinian G, Singh N, Weiswasser JM, Arora S. Evaluation of the microcirculation in vascular disease. *J Vasc Surg* 2005;42:574-81.
 29. Gubelin Harcha W, Barboza Martínez J, Tsai TF, Katsuoka K, Kawashima M, Tsuboi R, et al. A randomized, active- and placebo-controlled study of the efficacy and safety of different doses of dutasteride versus placebo and finasteride in the treatment of male subjects with androgenetic alopecia. *J Am Acad Dermatol* 2014;70:489-98.e3.
 30. Jeong SJ, Kwon GH, Chun J, Kim JS, Park CS, Kwon DY, et al. Cloning of fibrinolytic enzyme gene from *Bacillus subtilis* isolated from Cheonggukjang and its expression in protease-deficient *Bacillus subtilis* strains. *J Microbiol Biotechnol* 2007;17:1018-23.
 31. Paik JH, Yoon JB, Sim WY, Kim BS, Kim NI. The prevalence and types of androgenetic alopecia in Korean men and women. *Br J Dermatol* 2001;145:95-9.
 32. Park KS, Park DH. Comparison of *Saccharina japonica*-*Undaria pinnatifida* mixture and minoxidil on hair growth promoting effect in mice. *Arch Plast Surg* 2016;43:498-505.