

A Randomized, Double-Blind, Clinical Trial of the Effects of VitaBeard® on Facial Hair Growth in Healthy Adult Men

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Abstract

Although facial hair growth influences perceptions of attractiveness, it does not attract significant research dollars. VitaBeard® was the world's first facial hair-specific dietary supplement. The primary objective of this randomized, double-blind study was to assess the safety and efficacy of VitaBeard® on the rate of facial hair growth, facial hair thickness, total hair count and facial hair density. 48 healthy male subjects were assigned to high, mid, low dose or placebo for 33 days. Derscan was used to assess rate of facial hair growth at baseline and day 33. Facial hair count and density were assessed using Derscan and Trichoscan HD software. Blood work was done at baseline and day 33 for safety assessment. On a percentage change from baseline basis, the mid-dose IP group was 20% higher than placebo; an average increase of 11.8% compared to an average decrease of 8.9%, respectively ($p = 0.026$). The change from baseline in mean facial hair strand thickness showed a trend towards being lower in the low-dose group compared to placebo ($p = 0.071$). Although not statistically significant, mean thickness in mid-dose group was increased nearly two-fold more than placebo group and the group median shifted four times that of the placebo group. There were no safety concerns at any dose. Clinical trials registration is NCT03659994.

Keywords: Biotin; Vitamins; Facial Hair Growth; Facial Hair Thickness; Hair Count; Facial Hair Density; Beard Growth

Abbreviations

BMI: Body Mass Index; ICF: The Informed Consent Form; CFR: Code of Federal Regulations; ICH: The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; IP: Investigational Product; EOS: End of Study; GCP: Good Clinical Practices; REB: Independent Research Ethics Board; NNHPD: Natural and Non-Prescription Health Products Directorate; AEs: Adverse Events; MedDRA: Medical Dictionary for Regulatory Activities; LOCF: Last-Observation-Carried-Forward; CI: Confidence Intervals; DHT: Dihydrotestosterone

Introduction

Facial hair, or lack thereof, is not a subject that attracts significant interest or research dollars. Dixon and Brooks (2013) have reported that both men's and women's perceptions of facial hair affect how they perceive men's attractiveness, masculinity, parenting ability and general health [1]. These perceptions differ among the sexes, such that, for example, both men and women perceive a heavy stubble as most attractive, but only men consider a heavy beard to be as attractive as a heavy stubble. However, a heavy beard is closely associated with better parenting ability by women as well as men [1]. Facial hair is also linked to employment prospects, as reported by Lino de Souza, *et al* [2]. In their study, situated in Brazil, they reported that personnel managers preferred prospective new employees to be clean shaven and also found that beardedness was linked to older age and greater responsibility [2].

The issue of correcting a beard deficiency in men has not been addressed by researchers, except for a single publication in 1982 [3]. The researchers utilized enlarged photographs to quantify facial hair growth, and although they were able to correlate hair growth with

levels of androgens, they noted that nutritional factors may play a part in facial hair growth, or lack thereof. In addition to hormonal and nutritional factors, environmental factors can also play a role in the rate of facial hair growth [3].

Specific nutritional factors may potentiate the growth of beard hair. Most of these nutritional factors are targeted towards keratinocytes, the key cells in hair growth. Products high in silicon, calcium pantothenate, L-cystine and biotin, for example, have been targeted towards men with deficient facial hair growth [4]. In an *in vitro* study of one product containing all of these ingredients except for biotin, researchers assessed the effect of each ingredient, as well as the product as a whole, on human epidermal keratinocytes. They reported that L-cystine increased metabolic capacity by 8%, D-pantothenate enhanced metabolic capacity by 150% and the high-silicon ingredient increased metabolic capacity by 162% and stimulated cell proliferation by 215%. Together, the three ingredients increased metabolic capacity of the keratinocytes by 245%, although the statistical significance of these results was not reported [4].

The hair follicle extends down from the epidermis to the dermis, and the base of the follicle (the papilla) contains capillaries that supply nutrients to the keratinocytes. At the bottom of the papilla is the bulb, and the cells of the bulb divide every 23 to 72 hours, faster than any other cells in the body, so their nutritional needs are high [5]. In effect, hair requires a strong microcirculation in order to meet these nutritional needs. Both L-cystine and biotin are involved in the synthesis of keratin, a fibrous structural protein that is part of keratinocytes. In human hair, keratin is abundant, and is also found in harder products such as human nails [6,7].

There is repeated mention of B vitamins in electronic media, although there is no consensus with regard to the specific B vitamin(s) that might increase hair growth. For example, on one site, consumers are encouraged to incorporate vitamin B1, B6 and B12 into their diet in order to promote fast hair growth [8]. On another, biotin is highlighted for its ability to help improve hair quality and growth [9]. On one popular health-related website, pantothenic acid is cited as the favorable B vitamin to prevent hair loss and hair graying [10]. One supplement targeted to improve beard growth contains a variety of B vitamins, including biotin, B1, B2, B6 and B12, as well as pantothenic acid, L-methionine, L-cystine and a source of silicon [11].

In addition to nutritional factors, environmental factors, such as seasonal variation, can affect rate of human hair growth, including beard growth. Beard growth rate has been determined to be lowest during the winter months of January and February, after which time it is observed to increase, peaking during the month of July. The variability in beard growth during these months can be significant, such that July beard growth is, on average, 60% greater than in January and February [12].

When studying facial hair growth factors such as seasonality [12], testosterone levels [3], sleep deprivation [13] and dietary supplement intake [3] consideration must be given to provide robust and interpretable results. This study aimed to investigate multiple doses of a multivitamin supplement (VitaBeard®) containing biotin, as well as other vitamins, minerals and herbs that may support hair growth. The primary objective of this clinical trial was to assess the efficacy of the investigational product (IP), VitaBeard®, on the rate of facial hair growth. The secondary objectives of this clinical trial were to assess the efficacy of the IP on facial hair thickness, total hair count and facial hair density.

Materials and Methods

In this randomized, double-blind, parallel study design, 48 healthy adult males from the city of Guelph, Ontario, Canada (and surrounding communities), were recruited via social media, paper and email advertising to take part in this study, 47 completed. Inclusion criteria included healthy non-smoking men aged 18 - 40 with a body mass index (BMI) between 18.0 - 29.9 kg/m² (inclusive) who had dark (brown or black) facial hair with a Fitzpatrick skin type I-IV and good contrast between hair color and skin color. Subjects could not be taking prescription or non-prescription health products that may affect the study endpoint in the 6 months prior to visit 1 or during the study, such as hormone replacement therapy, anabolic steroids, chemotherapy, intravenous or oral B vitamins, 5 α -reductase inhibitors, medications with anti-androgenic properties, medications that can potentially cause hypertrichosis, oral glucocorticoids (inhaled glucocorticoids were permitted), lithium or phenothiazines, medications of known or suspected phototoxicity, as well as use of facial hair dyes, depilatories, waxing, plucking or bleaching or current or prior use at any time of laser hair removal on the target test or surrounding area.

Informed consent was obtained from subjects who satisfied the inclusion/exclusion criteria. The informed consent form (ICF) followed US 21 Code of Federal Regulations (CFR) part 50 and The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline E.6. Subjects were randomly assigned to one of four groups. Each group consumed a different dose of the investigational product (IP), i.e. 1, 2 or 3 capsules of IP or placebo per day. The duration of subject involvement was approximately 5 to 10 weeks, based on a screening period of up to 28 days, and a 33-day supplement period. Subjects visited the clinic on eight occasions, including two visits for screening (Visits 1a and 1b), three visits which formed the baseline evaluation (Visits 2a, 2b and 2c) and three visits at the end of the study (Visits 3a, 3b and 3c) to determine response to supplementation. Each subject received a small permanent ink marking under the chin at the second screening visit to provide a reference point to ensure images were captured of the same region at each study visit. At the beginning of the baseline and end of study (EOS) assessment period, subjects shaved the target region in the clinic with a disposable straight blade razor. A DermoScan (DermoScan GmbH, Regensburg, Germany) was used to capture an image of the area. After two days subjects returned to the clinic and the DermoScan used to capture an image of the target area. After three further days, subjects returned to the clinic and the DermoScan used to capture an image of the target area. Subjects refrained from shaving and drinking alcohol during the assessment periods. Subjects were instructed to take the IP with food for 33 days starting at the end of the baseline assessment period.

Each subject was instructed to take 3 capsules each day (one in the morning, one at noon and one in the evening) with food. Capsules were packaged in blister cards that included time of day on each blister to aid with compliance of dose timing. Packages for the low and mid-dose group contained 1 or 2 active capsules, respectively and the balance of the 3 capsules were made up of placebo capsules. All capsules were similar in size, shape and color to maintain blinding. Active capsules were taken in the morning only for low dose and morning and evening for mid-dose while high dose was morning mid-day and evening. Subjects on medications were instructed to take their study capsules a few hours before or after their other medication. Additionally, subjects were instructed to avoid taking capsules at bedtime. During the study period subjects were asked to avoid alcohol consumption 24 hours prior to the clinic visit and during the two 5-day assessment periods of facial hair growth. In addition, they were asked to maintain a stable body weight, activity level, sleep habits, sexual activity levels, time outdoors and dietary patterns as these activities have been shown to affect facial hair growth. They were asked to maintain current shaving habits during the study period and were asked to avoid shaving during assessment periods. Subjects were provided with daily diaries to record sexual activity, hours of sleep, hours spent outdoors, shaving habits and use of medications, including over the counter drugs and dietary supplements.

During the screening visit (Visit 1a) and Visit 3c (Day 33)/End of Study Visit, a blood sample was drawn for routine liver and kidney function tests, electrolytes, blood glucose (screening only for inclusion/exclusion purposes), serum testosterone and dihydrotestosterone, as well as for routine haematology.

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and consistent with GCP as required by the ICH Guideline E6, effective 17 January 1997. The study was submitted and approved by an independent Research Ethics Board (REB), Canadian SHIELD Research Ethics Board, Burlington, ON, Full approval was granted on 12 December 2016. Regulatory approval was obtained from Health Canada's Natural and Non-Prescription Health Products Directorate (NNHPD), Ottawa, Ontario on 09 November 2016. The clinical trials registration number is NCT03659994.

Assessment of the rate of facial hair growth after 33 days of supplementation

The primary efficacy assessment was measured by a DermoScan (DermoScan GmbH, Regensburg, Germany). The rate of facial hair growth was assessed as the change in hair length divided by the amount of time between images captured from Day -3 to Day 0 for baseline assessments and Day 30 to Day 33. To normalize the data, five hairs that were clearly identifiable in all 4 images were selected to assess length. Hairs selected were verified by a second researcher. One analyst performed the manual selection of the hairs using Trichoscan Smart software (DermoScan GmbH, Regensburg, Germany). One analyst ensured that there were no inter analyst variations with the manual selection. Once hairs were selected using the software, the system calculated the length of the hair. Data was entered into the electronic data capture system for the study which performed the final calculation of rate of growth. Rate of facial hair growth was determined as the change in length of facial hair from the time of the assessment on day 2 to the time of the assessment on day 5 for each assessment period (beginning of study and end of study) divided by the total time that had passed between the two assessments for the given assessment period.

Assessment of the facial hair count, density, length and thickness (hair strand width/diameter) in a predetermined area

Facial hair count and density were assessed using the DermoScan device and Trichoscan HD software. Calculations were automated by the software. To measure hair length and thickness (hair strand width/diameter), five hairs that were clearly identifiable in all images

were selected to assess length. Hairs selected were verified by a second researcher. One analyst performed the manual selection of the hairs using Trichoscan Smart software (DermoScan GmbH, Regensburg, Germany). One analyst ensured that there were no inter analyst variations with the manual selection. Once hairs were selected using the software, the system calculated the length and thickness of the hair. The same five hairs used to measure length were used to measure the hair strand thickness. The number of hairs and resulting density were automatically calculated by the Trichoscan Smart software.

Safety assessment

Safety assessments included routine blood chemistry and haematology, vital signs and biometrics assessed at various points throughout the study, as well as Adverse Events (AEs). An AE was defined as any sign, symptoms, syndrome, or illness that occurred or worsened during the use of a test article regardless of causality. Adverse events were coded using the Medical dictionary for regulatory activities (MedDRA) terminology version 20.0.

Statistical methods

For this study, ten subjects (10) per group were estimated to complete the study. With an expected attrition rate of 20%, twelve (12) subjects per group were therefore required for this study. In order to calculate sample size, the effect size (the expected amount of effect the product produces) for the product on the primary endpoint (i.e. rate of facial hair growth) is required as well as the variability around the effect size. As there were no previous studies with VitaBeard® or any similar products, a sample size calculation could not be performed. The study was designed with multiple dose groups to (i) understand the product's effect size and variability in response, and (ii) assess dose response which can provide a measure of efficacy of the product.

All subjects known to have taken ≥ 1 dose of study product and completed at least one post-baseline visit were included in the analysis of efficacy (modified intention-to-treat population) and all subjects known to have taken ≥ 1 dose of study product were included in the analysis of safety.

Missing values for primary and secondary endpoints at visit 3 were imputed using a last-observation-carried-forward (LOCF). No imputation was performed for any missing daily diary variables or missing values of safety variables. Rate of growth was unevaluable for two subjects due to an equipment error during data capture which did not permit calculation of hair length at visit 2b for one subject assigned to placebo and at visit 3c for one subject in the high dose group.

Laboratory data that were continuous in nature but were less than the lower limit of quantitation or above the upper limit of quantitation were imputed to the value of the lower or upper limit plus or minus one significant digit, respectively (e.g. if the result of a continuous laboratory test was < 20 , a value of 19 was assigned).

ANCOVA models included fixed effects for treatment group and the baseline covariates, as necessary. Similarly, within treatment group ANCOVA models were based on a mixed effects model with study subject as a random effect and fixed effects for study visit. Appropriate covariates were added to these models as sensitivity analyses.

Where endpoint variables differed significantly from parametric data modelling assumption, appropriate non-parametric models were implemented. In these situations, assessments of normality were based on an Anderson-Darling test. Non-parametric methods used included Wilcoxon test for treatment comparisons or signed-rank test for within group comparisons.

The differences in the least squares means between each treatment group and placebo, p-values are presented.

Blood parameters (hematology and clinical chemistry) were compared among groups using analysis of covariance using the screening value as the covariate. The dependent variable was the post-baseline value; the factor of interest was the treatment group (product) and value at screening (visit 1) was the covariate.

Statistical comparisons of adverse events were made using Fisher's Exact test or Chi-Square test as appropriate.

All statistical tests were 2-tailed and confidence intervals (CI) were set and 95%, p-values less than or equal to $\alpha = 0.05$ were considered statistically significant. Treatment was fitted as a categorical variable, using the placebo group as the reference group, and 95% confidence intervals were constructed around all estimated treatment differences. SAS® (SAS Institute Inc., Cary, NC) was used for programming of tables, figures, and listings.

Results and Discussion

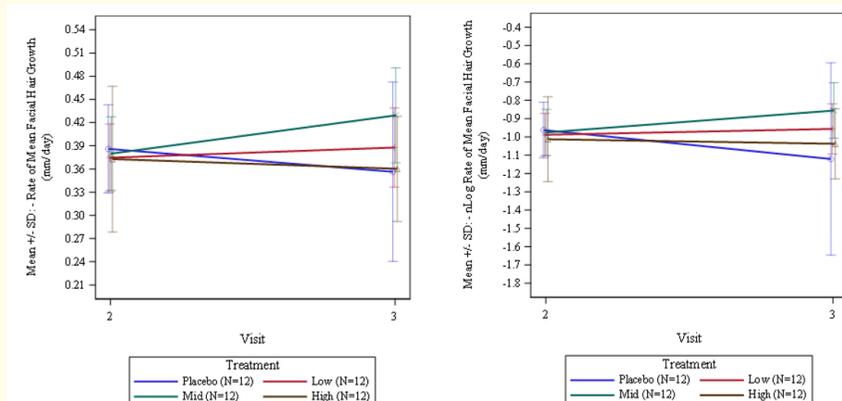
Results

Mean age was 23.8 and median age was 22, with a range of 18 to 40 years at screening. There were 41 white subjects, 4 Asian, 1 White/Asian, 1 African American/Black, and 1 White/African American/Black subject. Forty-seven (47) subjects were non-Hispanic/non-Latino, while one (1) was Hispanic/Latino/of Spanish origin. Twelve (12) subjects had black beard hair, and 36 had brown beard hair. Three (3) subjects had type I, 17 subjects had type II, 21 subjects had type III, and 7 subjects had type IV Fitzpatrick skin scale color. The overall rate of compliance with study product usage was high at an average of 97.5%. The minimum compliance rate was 79.0% and highest was 101.0% over the 33-day supplementation period.

The rate of mean facial hair growth change (See table 1) from baseline was significantly higher in mid-dose IP group compared to placebo ($p = 0.026$). This relationship was not observed in the low or high-dose IP groups. Figure 1 shows the change in rate of growth by group for raw data as well as natural log transformed data. On a percentage change from baseline basis, the mid-dose IP group was 20% higher than placebo; an average increase of 11.8% compared to an average decrease of 8.9%, respectively ($p = 0.026$) (See table 2).

	Placebo (N = 12)	Low (N = 12)	Mid (N = 12)	High (N = 12)
	[n] Mean ± SD Median (min, max)			
Visit 2c (Baseline)	[11] 0.39 ± 0.06 0.40 (0.29, 0.48)	[12] 0.37 ± 0.04 0.37 (0.32, 0.44)	[12] 0.38 ± 0.05 0.37 (0.30, 0.45)	[12] 0.37 ± 0.09 0.35 (0.26, 0.61)
Visit 3c (EOS)	[12] 0.36 ± 0.12 0.38 (0.07, 0.50)	[12] 0.39 ± 0.05 0.39 (0.29, 0.47)	[11] 0.43 ± 0.06 0.44 (0.32, 0.51)	[11] 0.36 ± 0.07 0.38 (0.27, 0.48)
Change from Baseline	[11] -0.03 ± 0.9 0.00 (-0.25, 0.08)	[12] 0.01 ± 0.05 0.01 (-0.05, 0.11)	[11] 0.04 ± 0.07 0.03 (-0.07, 0.16)	[11] -0.01 ± 0.10 -0.01 (-0.22, 0.15)
P-Value (Compared to Placebo)		0.233	0.026	0.701

Table 1: Rate of Mean Facial Hair Growth (mm/day).



*change in rate of growth by group for raw data as well as natural log transformed data is shown.

Figure 1: Rate of Mean Facial Hair Growth Prior to and After 33 Days of Supplementation.

	Placebo (N = 11)	Low (N = 12)	Mid (N = 11)	High (N = 11)
	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)
Percent Change from Baseline (%)	[11] -8.90 ± 26.41 0.48 (-78.44, 19.71)	[12] 4.24 ± 14.97 3.42 (-12.63, 32.62)	[11] 11.84 ± 19.85 7.57 (-15.29, 50.00)	[11] 1.32 ± 25.69 -2.35 (-35.95, 58.62)
P-Value (Compared to Placebo)	-	0.233	0.026	0.701

Table 2: Percent Change in Rate of Mean Facial Hair Growth (mm/day).

A natural logarithmic transformation was applied to data as the rate of growth may not be linear. There were no significant differences in facial hair count or density change from baseline between any of the IP groups and placebo (data not shown). Table 3 represents the average facial hair length in a predetermined area of the beard by treatment group after 3 and 5 days post-shaving before (Visit 2b and 2c) and after (Visit 3b and 3c) treatment. There were no significant differences in facial hair length change from baseline between any of the IP groups and placebo.

	Placebo (N = 12)	Low (N = 12)	Mid (N = 12)	High (N = 12)
	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)
Visit 2b	[11] 0.74 ± 0.26 0.69 (0.25, 1.13)	[12] 0.61 ± 0.29 0.55 (0.19, 1.23)	[12] 0.78 ± 0.25 0.81 (0.28, 1.11)	[12] 0.83 ± 0.35 0.81 (0.29, 1.50)
Visit 2c (Baseline)	[12] 1.89 ± 0.35 1.99 (1.15, 2.43)	[12] 1.76 ± 0.38 1.68 (1.34, 2.49)	[12] 1.95 ± 0.30 1.94 (1.36, 2.44)	[12] 2.07 ± 0.61 2.00 (1.50, 3.82)
Visit 3b	[12] 0.78 ± 0.32 0.80 (0.18, 1.32)	[12] 0.54 ± 0.33 0.49 (0.11, 1.13)	[11] 0.74 ± 0.44 0.58 (0.25, 1.81)	[12] 0.71 ± 0.27 0.67 (0.26, 1.17)
Visit 3c (EOS)	[12] 1.86 ± 0.45 2.00 (1.07, 2.36)	[12] 1.79 ± 0.37 1.74 (1.21, 2.34)	[11] 2.04 ± 0.33 1.99 (1.42, 2.56)	[11] 1.89 ± 0.48 1.80 (1.40, 3.10)
EOS (Change: Baseline to Visit 3c)	[12] -0.04 ± 0.29 -0.07 (-0.56, 0.46)	[12] 0.03 ± 0.25 0.05 (-0.31, 0.71)	[11] 0.08 ± 0.29 0.08 (-0.62, 0.39)	[11] -0.23 ± 0.25* -0.19 (-0.72, 0.09)
P-Value (Compared to Placebo)	-	0.738	0.228	0.197

Table 3: Mean Facial Hair Length after 3 (Visit 2b and 3b) and 5 Days (Visit 2c and 3c) of Growth Post-Shaving (mm).

The mean facial hair thickness change from baseline showed a trend toward being lower than placebo in low-dose IP group compared to placebo, although this did not reach statistical significance (p = 0.071) (See table 4). This relationship was not observed in the mid or high-dose IP groups. In the mid-dose group, the mean thickness was increased nearly 2-fold compared to the placebo group, and the group median shifted more than four times that of the placebo group. Changes seen in the mid-dose group were not statistically significant compared to placebo.

	Placebo (N = 12)	Low (N = 12)	Mid (N = 12)	High (N = 12)
	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)
Visit2c (Baseline)	[12] 143.40 ± 22.29 141.18 (100.25, 170.35)	[12] 132.59 ± 17.00 134.41 (93.15, 154.60)	[12] 135.00 ± 21.97 128.88 (101.56, 173.45)	[12] 127.64 ± 21.26 128.50 (85.49, 156.40)
Visit 3c (EOS)	[12] 150.75 ± 19.38 158.37 (110.55, 170.35)	[12] 136.43 ± 14.85 135.95 (96.80, 155.01)	[11] 150.06 ± 15.78 148.04 (124.80, 173.47)	[12] 137.83 ± 16.80 138.14 (109.89, 161.05)
EOS (Change Base- line to Visit 3c)	[12] 7.35 ± 10.60 2.69 (-0.16, 34.36)	[12] 3.84 ± 6.08 1.88 (0.00, 21.38)	[11] 13.04 ± 12.72 11.12 (0.02, 32.53)	[12] 10.19 ± 12.49 4.65 (-0.75, 31.13)
P-Value (Compared to Placebo)	-	0.071	0.318	0.603

Table 4: Mean Facial Hair Thickness (µm).

Serum testosterone and dihydrotestosterone (DHT) were measured in subjects as a tertiary exploratory endpoint. There was a trend toward a decrease in mean serum testosterone and DHT in subjects on the high-dose IP compared to placebo; however, a study with a larger sample size is needed to elucidate this relationship, as the standard deviation in these measures was large, and the trial sample size was not powered to evaluate this endpoint (See table 5).

	Placebo (N = 12)	Low (N = 12)	Mid (N = 12)	High (N = 12)
	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)	[n] Mean ± SD Median (min, max)
Total Testosterone (nmol/L)	[12] 6.34 ± 24.55 0.10 (-8.80, 83.60)	[12] -1.34 ± 2.54 -2.35 (-4.00, 4.10)	[11] -2.38 ± 6.14 -4.20 (-12.80, 9.40)	[12] -3.62 ± 1.99 -4.50 (-6.20, -0.30)
Dihydrotestosterone (pmol/L)	[11] 419.55 ± 1110.26 203.00 (-993.00, 2857.00)	[12] 48.58 ± 548.85 72.50 (-1147.00, 1014.00)	[11] 310.82 ± 1155.57 -2.00 (-1192.00, 2925.00)	[12] -255.55 ± 1244.29 -256.00 (-3304.00, 1862.00)

Table 5: Change from baseline in total testosterone and dihydrotestosterone.

Safety

There were eight incidences of AEs during the supplementation period, involving six subjects. One subject taking the low dose product had pruritis which the PI suspected was related to the product. The other seven AEs were not related to the investigational product.

There was no clinically significant chemistry, hematology or vital sign results during the testing phase of the products, indicating that the products tested are safe to consume over a 33-day period.

Discussion

The primary objective of this clinical trial was to demonstrate the efficacy of VitaBeard® in a randomized, placebo-controlled study with a proof of concept dose escalation design assessing the rate of facial hair growth after 33-days of supplementation. Additionally, this study was designed to account for factors that can affect facial hair growth between groups, including time spent outdoors, sexual activity, hours of sleep and dietary supplement intake.

The primary efficacy variable was the change from baseline in rate of hair growth at the end of the assessment period. In comparisons of each treatment group to placebo, there was a statistically significant finding. The rate of mean facial hair growth change from baseline was significantly ($p = 0.026$) higher in mid-dose IP group compared to placebo. In the mid-dose IP group, the average rate of facial hair growth increased by 0.04 ± 0.07 mm/day following supplementation, a 20% increase over placebo. Interestingly, the placebo group showed a -0.03 ± 0.9 mm/day or 8.9% decline in average rate of facial hair growth following supplementation over the study period from February to July 2017. This may partly be due to the seasonal decline in beard hair growth seen in the winter months in Northern climates [12]. Considering that the mid-dose IP group had an increased rate of facial hair growth compared to placebo, VitaBeard® may be able to promote beard hair growth to combat some environmental factors that are deterrents of hair growth, such as the seasonal decline in rate of beard hair growth. Given that several of the vitamins and minerals in VitaBeard® are known to be involved in the maintenance of healthy hair growth [14], this is not a surprising finding. Previous clinical research has shown the most significant benefit on hair growth endpoints from vitamin/mineral supplementation are where the subjects had micronutrient deficiencies at trial onset [14]. This may also be a factor in the present study considering that the estimated average requirements for vitamins A and D are not being met in approximately 50% and 90% of Canadian adult males (age 18 - 30), respectively [15]. However, serum levels of vitamins and minerals were not evaluated in the present trial, and conclusions related to improvements in micronutrient status cannot be drawn.

Secondly, the mean facial hair growth change from baseline was similar between the high dose IP group and placebo. This suggests that there is not a linear relationship beyond the mid-dose of VitaBeard® and rate of facial hair growth. Additionally, the high dose IP may not have a positive effect on facial hair growth in healthy adult males. It should be noted that the low dose active capsules were only taken in

the morning, while the mid-dose active was morning and evening, and the high dose was morning, mid-day and evening. It is possible that the mid-dose effectiveness has to do with the mid-dose timing; therefore, future studies should confirm timing of dosage.

There is a relationship between testosterone, DHT metabolism, and beard hair growth that appears to be unique to facial (non-scalp) hairs [16,17]. Previous research has shown that testosterone may promote facial hair follicle priming, while the metabolite, DHT, is thought to promote facial hair and beard growth [3]. In this trial, serum testosterone and DHT were measured in subjects as an observational measure. Notably, there was a trend towards a decrease in serum testosterone and DHT in subjects on the high-dose IP compared to placebo, suggesting that this dose may have a negative effect on serum testosterone and DHT levels. However, a study with a larger sample size is needed to elucidate this relationship, since the standard deviation in these measures was large, and the trial sample size was not powered to evaluate this endpoint.

Secondary efficacy variables included the change from baseline in facial hair count, density, length, and thickness (diameter) in a predetermined area. In comparisons of each treatment group to placebo, the change from baseline in facial hair count (Table 3), density (Table 4) and length (Table 5) did not significantly vary between these groups. It should be noted however, that in the mid-dose group, the mean thickness was increased nearly two-fold compared to the placebo group and the group median shifted more than four times that of the placebo group. Of note, the standard deviation of each measure was fairly high, suggesting that a larger sample size is needed to determine significant differences with the IP and placebo. Secondly, there was one finding for facial hair diameter that neared statistical significance. The mean facial hair thickness change from baseline showed a trend towards being lower than placebo in low-dose IP group compared to placebo, although this did not reach statistical significance ($p = 0.071$). This relationship was not observed in the mid or high-dose IP groups. An increase in facial hair thickness may be an indicator that facial hairs are becoming more terminal than vellus in nature, and thus contribute to the thickness of the beard. Further research is required to determine the effect on hair strand thickness.

This study was the first clinical trial to evaluate the efficacy of VitaBeard®, or any other dietary supplement, on parameters of facial hair growth and safety. Although there was no obvious linear dose response on the primary and secondary efficacy endpoints evaluated, the doses studied provided meaningful information. Specifically, the low to mid-dose of VitaBeard® showed efficacy on the rate of facial hair growth, respectively, while the high-dose did not differ from placebo for any endpoint. The current study suggests the optimal dose of VitaBeard® is 1 capsule taken twice daily (once in the morning and once in the evening, with food). The varying results between groups could be a factor due to dosing time, as the low dose group received one active capsule every 24 hours, the mid-dose group received two VitaBeard® capsules daily separated by approximately every 12 hours, and the high dose group received 3 VitaBeard® capsules daily separated by 4 - 6 hours, followed by a span of approximately 12 hours per day. Future studies evaluating the efficacy of VitaBeard® on beard growth parameters might include investigating the pharmacokinetics and pharmacodynamics of the product or include one dose lower than the lowest dose in this study to assess linearity using three doses. Further, it may be warranted to assess the nutrient status of subjects as part of screening procedures in future studies. Investigation on other parameters of beard growth, such as hair thickness, could be considered, and sample size could be determined based on the results of the current study in order to achieve statistically significant results.

Conclusion

This study was the first clinical trial to evaluate the efficacy of VitaBeard® on parameters of facial hair growth and safety. Statistical significance was found on the rate of mean facial hair growth change from baseline in mid-dose IP group compared to placebo. Although there was no obvious linear dose response on the other primary and secondary efficacy endpoints evaluated, the doses studied provided meaningful information for future study. Specifically, the low to mid-dose of VitaBeard® showed efficacy on mean facial hair thickness and the rate of facial hair growth, respectively, while the high-dose did not differ from placebo for any endpoint. Taken together, future studies evaluating the efficacy of VitaBeard® on beard growth parameters should evaluate the low to mid- dose of VitaBeard®. Data from this study should be used to determine the appropriate sample size needed to robustly evaluate these efficacy parameters.

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Conflict of Interest

Joshua Baisley, Anna De Boer, Anthony Bier and Susan Hewlings are employed by Nutrasource Diagnostics, the Contract Research Organization that conducted the trial.

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