Research Article

Evaluating the Therapeutic Potential of Fish Collagen Peptide and Bovine Collagen Peptide Supplementation in the Skin, Nail, and Hair Health Improvement: A Double-Blinded, Placebo-Controlled Clinical Study

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Abstract

Nutraceuticals are foods or ingredients with defined physiological effects, administered to improve health status without adverse effects. Nutritional supplements are products designed to provide essential nutrients that may be lacking or insufficient in an individual's diet. Collagen supplements maintain skin, hair, nails, and body tissue health. Collagen, the most abundant protein in the body, is a crucial component of connective tissue and plays a key role in joint & bone health. It offers structural support to the extracellular space of connective tissues and is the ideal matrix for skin, tendons, bones, and ligaments. Collagen peptides (CP), including Fish Collagen Peptide (FCP) and Bovine Collagen Peptide (BCP), have been shown to exert a beneficial effect on skin, muscles, bone health, hair, and nail maintenance.

Titan Biotech Limited, India, conducted an independent, third-party-based, double-blinded, placebo-controlled clinical study to verify the efficacy and safety of their FCP and BCP. A total of 78 participants between 18 and 45 years of age were enrolled in this study and randomly divided into three groups: FCP, BCP, and a placebo (PB) group. The study spanned over 90 days and

involved the daily oral administration of 5g FCP, 5g BCP, or 5g PB. 60 Second Hair Count Test, Skin Improvement Questionnaire, Hair Growth Questionnaire, and Nail Health Questionnaire were employed to evaluate the efficacy of collagen peptide supplementation in the Skin, Nail, and Hair Health Improvement.

FCP showed a reduction of 26.75% in 60HCT, while BCP and Placebo showed a reduction of 19.79% and 1.79%, respectively. After 90 days, FCP scored an average of 22.67 on the Skin Improvement Questionnaire, 22.29 on the Hair Growth Questionnaire, and 22.83 on the Nail Health Questionnaire. BCP scored an average of 19.15, 19.38, and 19.42, respectively. Both performed better than PB in all evaluations.

In conclusion, the clinical study findings suggest that both BCP and FCP supplementation hold promise as nutraceutical therapies in improving Skin, Nail, and Hair Health. CP supplementation is a safe and effective nutraceutical option that improves skin, hair, and nail health and overall quality of life for individuals.

Keywords: Collagen peptide, Bovine collagen, Fish collagen, Collagen for skin, Collagen for nails, Collagen for hair

Introduction

The skin, the largest organ in the human body, acts as a barrier between internal and external environments, consisting of three layers: epidermis, dermis, and hypodermis, protecting the body from mechanical, chemical, microorganism, and ultraviolet damage [1]. Skin's surface texture, color, physiological properties, and environmental factors like UV irradiation and free radicals influence skin's appearance. It plays a role in immune system function and well-being [2]. Intrinsic and extrinsic processes, including external factors like smoking, sun exposure, poor nutrition, and excessive alcohol consumption, influence skin aging [3]. Psychological stress occurs when individuals feel pressure exceeds their adaptive capacity, leading to physiological and behavioural changes to adapt to the stress. Skin, the largest organ in the body, is a target of stress responses and an immediate stress perceiver. Skin plays a crucial role in immune and barrier functions, maintaining homeostasis between the external environment and internal tissues [4]. UV radiation is an essential environmental factor in air pollution, causing skin damage and aging. Pollution damages the ozone layer, enhancing the effects of free radicals and UV radiation on the skin, making it the most damaging particulate matter [5]. Moreover, it also triggers the

development of melanin, which contributes to skin discoloration [6].

Hair has psychological and sociological importance for an individual. Women, in particular, have adapted their appearance through hair colour or style, which can be straight, wavy, curly, blonde, black, brown, or red. These natural variations are crucial to our identity, influenced by fashion, culture, and society [7]. Hair loss is a common complaint among dermatologists and often leads to severe psychological disturbances and depression symptoms. Diagnosis involves a detailed clinical history, physical exam, diagnostic tests, laboratory testing, and scalp biopsy. The pathophysiology of hair loss disorders can include infectious, nutritional, congenital, autoimmune, or environmental causes [8]. Hair loss affects 50% of males and 25% of females globally and is often seen as an abnormality or failure to conform to societal standards. Women face immense psychological and social stress, contributing to hair loss among young women [9]. Hair loss in older women can be caused by psychological stress (30%), fever (33%), abortion (21%), trauma (13%), and hypothyroidism (10%). Over 50% of women had multiple causes, while 6% could not be

determined [10].

Healthy nails are crucial for women's daily work and appearance, with a growing market for nail cosmetics. However, 99% of people will experience a nail disorder, the main complaint in 10% of dermatology visits. Healthy nails are shiny, smooth, and uniform, with attached cuticles, nail folds, and plates. They are not cracked, rigid, or broken and have a pink visible nail bed and white free margin. Desirable characteristics include a free edge that extends beyond the bed, a shiny surface, and a slight curve on the free-margin view. Healthy grooming habits include cutting fingernails straight across and rounding the edges. Brittle nails often develop due to impaired water-binding capacity, possibly due to abnormalities in keratin, keratin-associated proteins, or lipid content [11]. Nail disorders affect 99% of people and account for 10% of all medical visits to dermatologists in the US. Women often seek medical intervention for nail disorders caused by nail cosmetics, grooming complications, and aging. Nail plate brittleness affects up to 20% of the population, particularly women over 50, with fingernail fragility being more prevalent than toenail fragility. Nail brittleness results in nails splitting, flaking, crumbling, becoming soft, and losing elasticity [12].

An emerging positive effect of oral collagen peptide intake has received much attention. Collagen peptides are highly digestible and absorbable; more than 90% of collagen peptides are available & digested as small peptides in the bloodstream within one hour. There is much clinical evidence for the efficacy of specific collagen peptides (Fish and Bovine sources) to improve skin moisture [13]. Collagen supplements maintain the skin, hair, nails, and body tissues. The collagen metabolites attract fibroblasts that generate new collagen synthesis, thereby aiding in assembling bone, skin, and ligaments [14]. The objective of this clinical study was to determine the efficacy and safety of Bovine Collagen Peptide (BCP) and Fish Collagen Peptide (FCP) in comparison with Placebo (PB) in a double-blinded study design.

Materials and Methods

Study design

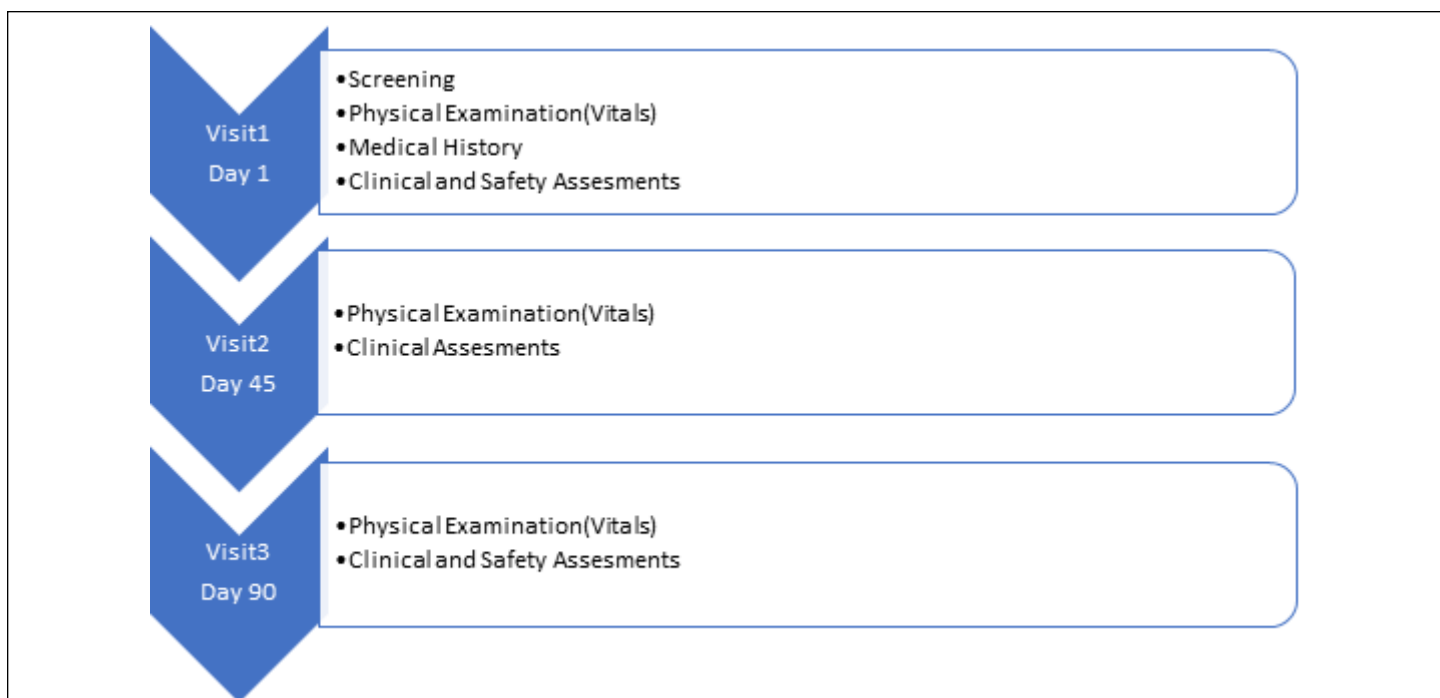This clinical trial was managed by Aurous Healthcare R&D India

Figure1: Schematic Representation of the study Design.

Pvt Ltd (Chennai). The study was designed as a 90-day double-blind, prospective, randomised, placebo-controlled clinical study to evaluate the efficacy, safety, and tolerability of BCP and FCP of Titan Biotech Pvt. Ltd. as a nutraceutical Supplement for Skin, Nail, and Hair Health improvement. The study was reviewed and approved by the Universal Ethics Committee, Chennai CDSCO registered Ethics Committee (Reg no. ECR/125/Indt/TN/2013/RR-20) and OHRP, USFDA (Reg no. IORG0007234) before the conduct of the study. The clinical study was further registered with the Clinical Trial Registry of India, holding registration no CTRI/2019/06/019857 dated 26-Jun-19. The study was conducted at Raam Clinic, Chennai. Figure 1 illustrates the study design, and Table 1 lists the procedures and observations at each time point. A total of 78 adult subjects between the ages of 18 and 45 years (both sexes and ages inclusive) were screened for the clinical study. Subjects who fulfilled the study criteria were enrolled in the study. The enrolled subjects were randomized into three treatment arms in a 1:1:1 ratio. The study design is outlined in Table 2.

On the first day of treatment, an informed consent process was undertaken, and then demographic details and significant medical and surgical history were noted. Vital signs like pulse rate, Respiratory rate, body temperature, and blood pressure were checked and noted. Baseline Safety Assessments such as Complete blood count and serum biochemistry levels were assessed. The clinical assessments, such as the 60-second hair count test, were administered as a baseline evaluation. Subjects received the investigational product either 5g BCP, 5g Collagen peptide FCP, or 5g Placebo as per the randomization list. Subjects consumed the investigational product (powder) orally once a day for 90 days. On day 45 of treatment, Vital signs were checked and noted, improvement metrics were assessed using a 60-second hair count test, Skin improvement questionnaire, hair growth questionnaire, and nail health questionnaire. On Day 90 (the last day of treatment), Vital signs were checked and noted. Final improvement metrics were analyzed. The 60-second Hair Count Test, Skin Improvement Questionnaire, Hair Growth Questionnaire, and Nail Health Questionnaire were assessed. Safety assessments such as Complete Blood Count and Serum Biochemistry were also evaluated.

Removal of subjects from therapy or assessment:

Subjects No 199018, 199035, 199059, and 199073 were lost follow-up due to personal reasons. They did not continue in the study. No subject withdrew due to adverse event or due to clinical judgment.

Randomization:

The enrolled subjects were randomized and allotted to three arms of this clinical study in a 1: 1: 1 ratio in a double blinded fashion. To protect blinding, similar containers were used with coded labels. Neither the patient, investigator, and research staff should have known which test compound the subject was assigned. This study does not allow any standard therapy.

Efficacy and safety variables

Blood tests: Blood samples (approximately 10 ml) were withdrawn for safety assessments of CBC, LFT, and RFT at the start and end of the treatment period.

Appropriateness of measurements: 60 Second Hair Count test is a standardized test to verify hair fall before and after Treatment. All other questionnaires were designed in a non-biased format for this study and used a 5-point Likert scale. It was done to record the subject's perspective on treatment-related improvement and quality of life.

Statistical methods:

The primary objective of this clinical study was to confirm the effectiveness of two types of Collagen peptides (Fish Source and Bovine Source) in comparison with Placebo in the improvement of Skin, Hair, and Nail Health. The primary efficacy analysis was summarized and analyzed using Per Protocol Analysis. Safety endpoints were summarized and analyzed using the Safety Analysis Set. Efficacy analysis was done based on improvements from baseline on assessments – 60 Second Hair Count Test, Skin Improvement Questionnaire, Hair Growth Questionnaire, and Nail Health Questionnaire. The statistical testing was performed at the $p=0.05$ significance level (Single and two proportional tests). This was a confirmatory study, so no adjustments were made for multiple comparisons. After unblinding and completing the entire

Table 1: Schedule of events			
PARTICULARS	**VISIT 1** Screening Enrolment& Randomisation **Day 01**	**VISIT 2** Improvement Matrics **Day 45**	**VISIT 3** Improvement Matrics & End of Study **Day 90**
Informed Consent Process	✓	✗	✗
Demographic Data Capture	✓	✗	✗
Recording of Vital Signs ^	✓	✓	✓
Physical Examination	✓	✓	✓
LABORATORY INVESTIGATIONS			
Complete Blood Count	✓	✗	✓
Serum Biochemistry	✓	✗	✓
EFFICACY ASSESSMENTS			
60 Second Hair Count Test	✓	✓	✓
Skin Improvement Questionnaire	✗	✓	✓
Hair Growth Questionnaire	✗	✓	✓
Nail Health Questionnaire	✗	✓	✓
INVESTIGATIONAL PRODUCT MANAGEMENT			
Dispensing of IP &IPCC	✓	✓	✗
Returning of unused IP and filled IPCC	✗	✓	✓
SAFETY MONITORING			
Adverse Event Recording	✓	✓	✓
Concomitant Medication Record	✓	✓	✓
✓ = Activities to be **Done** on said visit			
✗ = Activities to be **Not Done** on said visit			
^ Vital signs = Blood Pressure (Sitting Arm), Temperature, Pulse Rate, Respiratory Rate			

Table 2: Inclusion and exclusion criteria.
INCLUSION CRITERIA
1. Adults between 18 and 45 years of age (both ages and all sexes inclusive)
2. Subjects with any skin type with a minimum of one concern i. Wrinkles   ii. Dry, Dull Skin iii. Brittle Nails   iv. Dry, Dull Hair v. Hair Fall, Breakage   vi. Split Ends of the hair
3. Subject/LAR who is willing to give informed consent for participation, able to comprehend and understand the responsibilities during treatment period and follow up period.
4. Subjects who are willing not to participate in any other clinical trial during participation in the current trial.
EXCLUSION CRITERIA
1. Subjects with known hypersensitivity to investigational product or its constituents.
2. Subjects who have skin condition that prevent proper examination or evaluation of study criteria.
3. Subjects who are on active treatments for skin and/or hair conditions.
4. Subjects who have dyed their hair in the last 60 days.
5. Subjects with immunocompromised state complications.
6. Any significant medical condition (e.g., significant psychiatric or neurological disorders, active alcohol/drug abuse, etc.), any medical condition that is unstable/poorly controlled or other factor (e.g., planned relocation) that the Investigator felt would interfere with study evaluations and study participation.
7. Females who are pregnant or lactating or planning to become pregnant during the study period.
8. Subjects who mentally unable to comprehend the responsibilities and adhere to the stipulations of the protocol.
9. Subjects, who in the opinion of the Investigator or the Medical Experts are not eligible for enrolment in the study.

study, treatment groups summarized all the data for this clinical study report. Change from baseline in study-specific parameters was analyzed using an Analysis of Variance (ANOVA) method with the treatment group as fixed factors. The analyses were performed using SAS V 9.1.3. The 95% confidence interval around the percentage mean change from baseline to end of treatment period was constructed.

Results

Baseline statistics and compliance of trial subjects

Screened subjects were evaluated for inclusion criteria, exclusion criteria, medical history, concomitant medications, vital signs, physical examination, smoking habits, and alcohol consumption. The Demographic & baseline characteristics of patients are summarized in Table 3.

Skin improvement questionnaire

Subjects on BCP scored 19.15 (SD 2.09), and Subjects on FCP scored 22.67 (SD 0.55) in 90 days of treatment. FCP performed better than BCP in improving Skin Health; however, both

Table 3: Demographic and baseline characteristics of the trial subjects			
	Collagen (Bovine)	**Collagen (Fish)**	**Placebo**
Gender	**Female** 15 (58%) **Male** 11 (42%) **Total** 26 (100%)	**Female** 13 (50%) **Male** 13 (50%) **Total** 26 (100%)	**Female** 8 (31%) **Male** 18 (69%) **Total** 26 (100%)
Age	36.58 ± 6.60	33.15± 8.35	30.62 ± 7.84
Height	1.65± 0.08	1.67 ± 0.08	1.66 ± 0.07
Weight	78.29± 6.75	77.33± 6.37	77.47± 6.62
BMI	29.01 ±3.36	27.99± 3.36	28.36 ±3.60
Pulse Rate	79.96± 5.80	81.46 ±6.34	78.92± 6.99
Respiratory rate	20.35 ±3.60	20.08 ±3.53	18.73± 3.40
Temperature	97.36± 0.82	97.45 ±0.69	97.50± 0.65
Systolic BP	115.54± 7.90	117.81± 8.50	115.27± 7.09
Diastolic BP	82.69 ±5.70	80.96± 8.25	82.69± 7.78
Values are expressed as mean ± SD			

Baseline, Day 45 and Day 90 is given in Figure 2.

60-Second hair count test (60SHCT)

Subjects on BCP showed a improvement of only 19.79% (SD 1.90%), and Subjects on FCP showed a improvement of 26.75% (SD 1.47%) in hair fall from baseline 60SCHT scores in 90 days of treatment. FCP performed better than BCP in reducing hair fall; however, both performed better than PB 1.79% (SD 0.95%). Comparison of 60 second Hair Count Test scores of each treatment group Baseline, Day 45 and Day 90 is given in Figure 3.

Hair growth questionnaire

Subjects on BCP scored 19.38 (SD 0.68), and Subjects on FCP scored 22.29 (SD 0.64) in 90 days of treatment. FCP performed better than BCP in improving Hair Health and growth; however, both performed better than PB 7.32 (SD 0.47). Comparison of Hair Growth Questionnaire scores of each treatment group Baseline, Day 45 and Day 90 is given in Figure 4.

| Table 4: Summary of efficacy assessments.				
Assessments	**Visits**	**Collagen (Bovine)**	**Collagen (Fish)**	**Placebo**
60 Second Hair Count Test	**Day 1**	49.88 ± 8.52	49.42 ±9.46	45.05± 7.12
	Day 45	43.69 ±7.47	40.52± 7.66	42.66± 7.46
	Day 90	40.01± 7.17	36.20 ±7.16	44.24± 7.04
Skin Improvement Questionnaire	**Day 1**	N/Ap	N/Ap	N/Ap
	Day 45	13.92 ±1.02	16.88± 1.19	5.59± 0.67
	Day 90	19.15± 2.13	22.67 ±0.56	7.32 ±0.48
Hair Growth Questionnaire	**Day 1**	N/Ap	N/Ap	N/Ap
	Day 45	14.19 ±0.80	16.79 ±0.93	6.09 ± 0.97
	Day 90	19.38 ±0.70	22.79 ±0.66	7.32 ± 0.48
Nail Health Questionnaire	**Day 1**	N/Ap	N/Ap	N/Ap
	Day 45	14.04± 1.15	16.83± 1.09	5.55± 0.74
	Day 90	19.42 ±0.50	22.83 ±0.64	7.41± 0.50
Values are expressed as mean ± SD.				
N/Ap = Not Applicable				
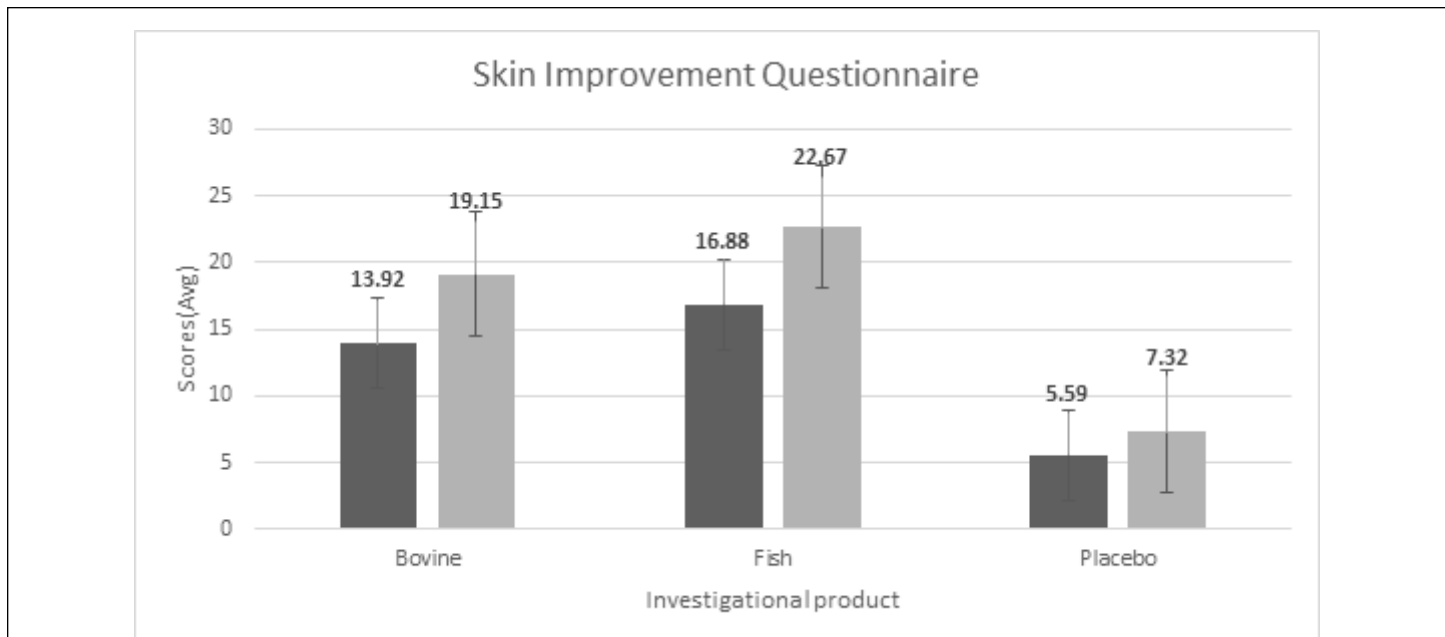
Figure 2: Changes in Skin Improvement Questionnaire scores at Day 45 and 90 from baseline. Skin Improvement Questionnaire scores from each treatment group were compared to baseline value at specified time points.
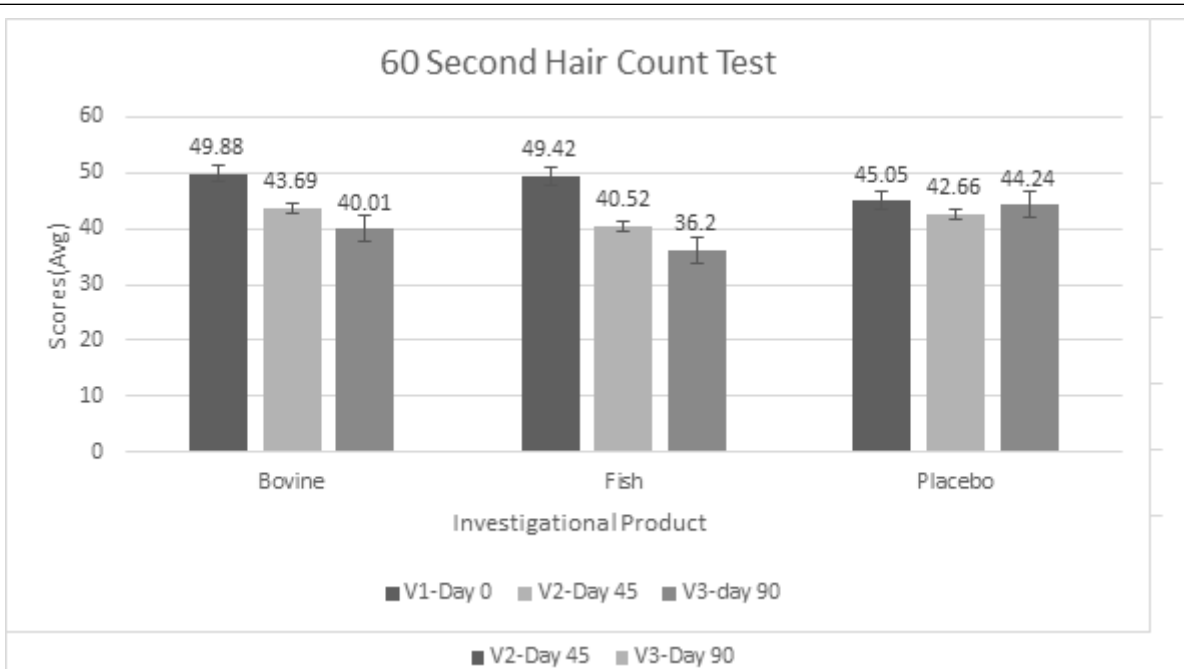
Figure 3: Changes in 60 Second Hair Count Test scores at Day 90 from baseline. 60 Second Hair Count Test scores from each treatment group were compared to baseline value at specified time points.
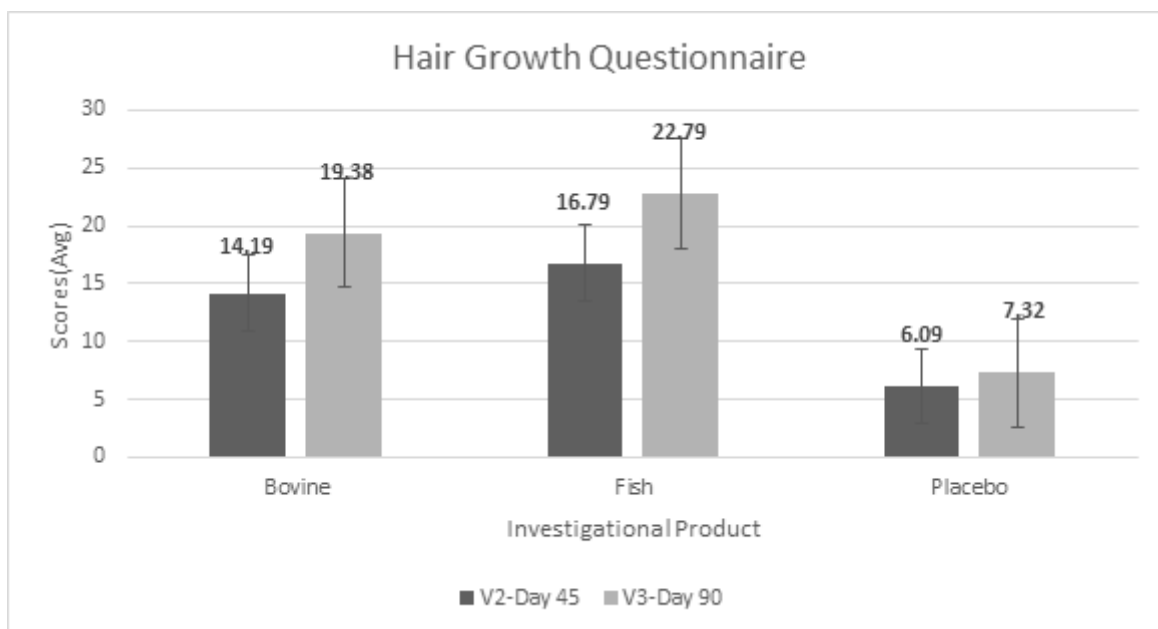

Figure 4: Changes in Hair Growth Questionnaire scores at Day 45 and 90 from baseline. Hair Growth Questionnaire scores from each treatment group were compared to baseline value at specified time points.
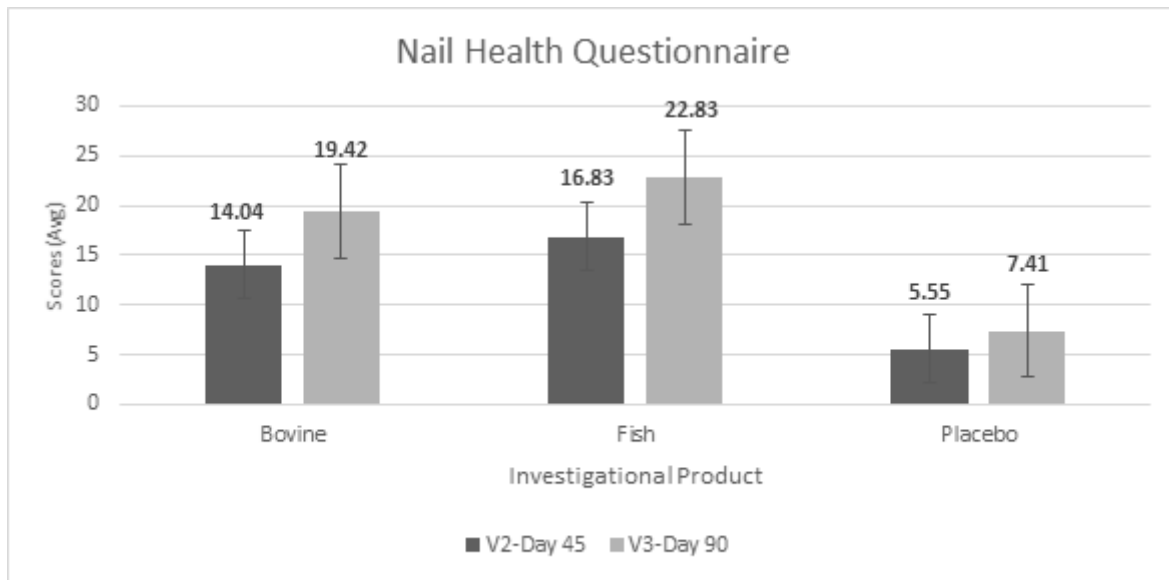
Figure 5: Changes in Nail Health Questionnaire scores at Day 45 and 90 from baseline. Nail Health   Questionnaire scores from each treatment group were compared to baseline value at specified time points.

performed better than PB 7.32 (SD 0.47). Comparison of Skin Improvement Questionnaire scores of each treatment group Baseline, Day 45 and Day 90 is given in Figure 2.

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Subjects on BCP scored 19.38 (SD 0.68), and Subjects on FCP scored 22.29 (SD 0.64) in 90 days of treatment. FCP performed better than BCP in improving Hair Health and growth; however, both performed better than PB 7.32 (SD 0.47). Comparison of Hair Growth Questionnaire scores of each treatment group Baseline, Day 45 and Day 90 is given in Figure 4.

Nail health questionnaire

Subjects on BCP scored 19.42 (SD 0.49), and Subjects on FCP scored 22.83 (SD 0.62) in 90 days of treatment. FCP performed better than BCP in improving Nail Health; however, both performed better than PB 7.41 (SD 0.49). Comparison of Nail Health Questionnaire scores of each treatment group Baseline, Day 45 and Day 90 is given in Figure 5.

Adverse events

 No adverse events were reported in the clinical study. The safety investigations also showed no significant/ abnormal clinical difference from baseline to the end of the study.

Discussion

As individuals age, the production of collagen in their bodies decline resulting in reduction of tissue thickness, strength, and flexibility. To counteract this, collagen supplements have been formulated to improve the skin, hair, nails, and body tissues of individuals. These supplements attract fibroblasts, which stimulate the production of new collagen, thereby aiding in the formation of

bone, skin, and ligaments. Moreover, they enhance the diameter and cohesion of collagen fibres within the dermis, contributing to the development of collagen fibrils [15]. Collagen peptides (CPs) are considered vital active components due to their diverse bioactivities, high bioavailability, and excellent biocompatibility. These peptides are derived from the enzymatic breakdown of collagen or gelatin. Several studies have demonstrated the beneficial effects of CPs ingestion on skin, these effects include the improvement of moisture retention ability and the repair of endogenous collagen and elastin protein fibers. Additionally, clinical trials have provided evidence of the positive effects of CPs intake on facial skin. These effects encompass the enhancement of facial skin elasticity, reduction of skin dryness and wrinkles, and an increase in collagen content within the skin dermis [16]. These peptides are considerably abundant in glycine, proline, and hydroxyproline amino acids. Numerous experiments have provided evidence of the efficient absorption and distribution of collagen peptides to the dermis [17].

This study suggests supplementation with Bovine or Fish Collagen Peptide improves Skin, Hair, and Nail Health in Adults. By the end of the study, BCP and FCP showed a significant reduction in hair fall, as demonstrated by the reduction of hair fall % in 60 Second Hair Comb Test. Fish Collagen and Bovine Collagen promote skin hydration and moisture retention, potentially support hair growth by improving collagen in the scalp and hair follicles, and work on brittle nails by strengthening nail beds and making them less prone to chipping. FCP and BCP performed better in all performance outcomes (p<0.05) than Placebo. The summary of all the efficacy assessments citing the scores from all the visits is given in Table 4.

The subject reported improved hair and nail health after consuming FCP and BCP for 90 days. It significantly boosted the participants' confidence, positively impacting their everyday quality of life. It is important to note that our study's BCP & FCP supplementation was well-tolerated, with no significant adverse effects reported. The absence of adverse events supports the potential use of collagen peptide supplementation as a nutraceutical aid to improve skin, hair, and nail health. Throughout the study, the subjects were instructed to continue with the same lifestyle without making any significant dietary changes, exercise regimens, or routines as before enrolment in this study to be able to evaluate the real-time effectiveness of BCP & FCP. The study has no sources of potential bias, imprecision, and multiplicity of analyses. The study inclusion and exclusion criteria have been designed to include subjects within a wide age range, including subjects of all genders, socio-economic status, and demographics, in an attempt to be objective and yet external validity, generalizability, and applicability.

Conclusion

In conclusion, our randomized clinical trial provides promising evidence regarding the potential benefits of Bovine Collagen Peptide and Fish Collagen Peptide Supplementation in improving Skin, Hair, and Nail Health. With such encouraging results, it is safe to say that collagen peptide supplementation as part of everyday life would replenish the natural collagen depleting with age and help rebuild the skin's structural integrity, improving hair and nail health.

Conflict of Interest

None declared.

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