CLINICAL STUDY SUMMARY

Confidentially Prepared for:
Vinh Hoan Corporation
National Road 30, Ward 11, Cao Lanh City,
Dong Thap Province, Vietnam

Date: February 1, 2018

KGK Science Inc.
255 Queens Avenue
Suite 1440
London, Ontario
Canada N6A 5R8

Qualified Investigator
Tetyana Pelipyagina, M.D.

Table of Contents

List of Figures

List of Tables

Introduction

Objective: This study investigated changes in skin elasticity, skin hydration, skin wrinkles, and participant self-reported skin parameters after 12 weeks of Vinh Wellness Collagen (VWC) supplementation.

Study design:	Single-center, randomized, double-blind, placebo controlled 2-arm parallel
Duration:	12 weeks / 84 days
Number of participants:	50 enrolled – intent to treat (ITT) population (25 participants randomized equally to each study arm at ratio of 1:1) 36 per protocol (PP) population (17 from Vinh Wellness Collagen group and 19 from placebo group analyzed)
Demographics:	Female 45-60 years of age BMI 19.9-31.2 kg/m^2 90% Western European White
Active ingredient:	Hydrolyzed collagen (10 g/day)
Placebo:	Maltodextrin powder (10 g/day)
Data points:	<u>Primary outcome:</u> The difference in cheek skin elasticity, measured as R2, between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks. <u>Secondary outcomes</u>: 1. The difference in underarm skin elasticity between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks 2. The difference in cheek skin hydration between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks 3. The difference in nasolabial wrinkles between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks

4. The difference in skin quality VAS scores between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks

5. The difference in cheek skin elasticity, measured as R5, between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks

6. The difference in cheek skin elasticity, measured as R7, between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks

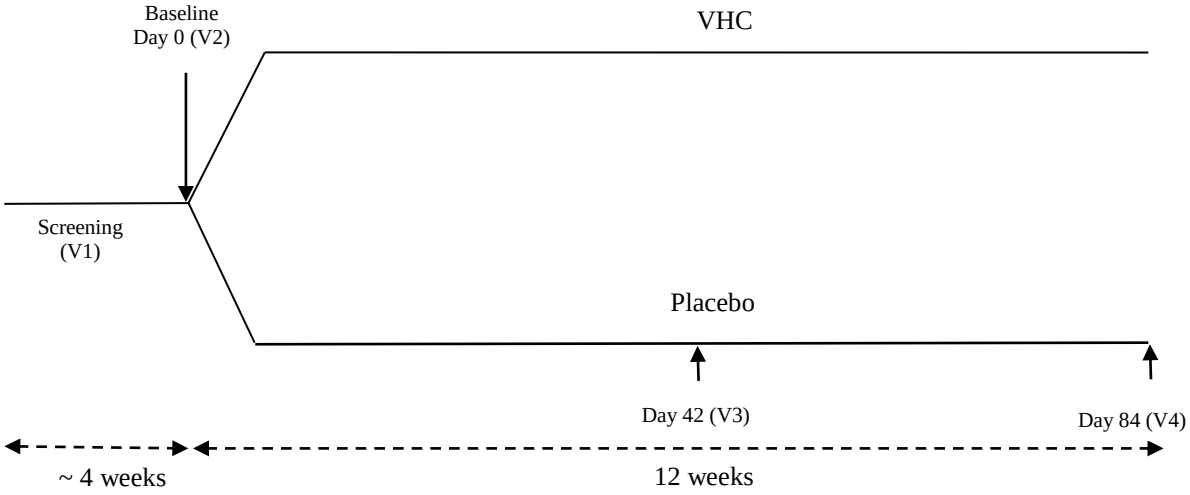
7. The difference in cheek skin elasticity, measured as Q3, between Vinh Wellness Collagen and placebo-supplemented participants after 12 weeks

Safety outcomes:

1. The difference in vital signs (blood pressure, heart rate) weight, BMI, hematology, complete blood count (CBC), liver function (AST, ALT, bilirubin), and kidney function (Na, K, Cl, creatinine, eGFR) between Vinh Wellness Collagen and placebo groups

2. The incidence of adverse events in the Vinh Wellness Collagen and placebo groups

Figure 1: Study Flow Diagram



Results

Safety

Vital signs and anthropometrics were measured at each study visit while laboratory parameters for all safety endpoints were assessed at screening and end-of-study visits.

At 12 weeks, Vinh Wellness Collagen supplementation at a dose of 10 g/day was found to be safe as assessed by adverse events, vital signs, anthropometrics measures, complete blood count, and liver and kidney markers. The safety of Vinh Wellness Collagen in the current study strengthens the available evidence for its use in a healthy population.

For a detailed list of parameters assessed, please see Safety outcomes above.

Hematology and Clinical Chemistry

All blood safety parameters for complete blood count, electrolytes, liver and kidney markers were found to be not clinically relevant by the qualified investigator following the 12-week supplementation period. Between the two groups, the lymphocyte count increased significantly in the placebo group compared to the Vinh Wellness Collagen group. There were no significant differences within the Vinh Wellness Collagen and placebo groups except for a significant difference between screening and end-of-study in the mean corpuscular hemoglobin parameter in all participants. All excursions between and within the two groups in hematology, chemistry, electrolytes, and liver and kidney function markers remained within healthy clinical reference ranges as per the opinion of the qualified investigator.

Vital Signs and Anthropometric Measurements

There were no significant differences between or within the two groups in vital signs (blood pressure, heart rate) and anthropometric measurements (weight, BMI) of participants at weeks 6 and 12 compared to baseline. All excursions in vital signs and anthropometric measurements were deemed not clinically relevant by the Qualified Investigator.

Adverse Events (AEs)

A total of 32 AEs were reported by 19 participants, including 18 AEs from participants in the Vinh Wellness Collagen group and 14 AEs from participants in the placebo group.

Of the 18 AEs reported in the group consuming Vinh Wellness Collagen, 5 were reported as being not related and 12 were reported as being unlikely to be related. A mild intensity nausea was the only AE reported as being possibly related. No AEs were reported as being probably related or most probably related to the intake of Vinh Wellness Collagen.

Of the 14 AEs reported in the group consuming placebo, 6 were reported as being not related and 8 were reported as being unlikely to be related. No AEs were reported as being possibly, probably, or most probably related to the intake of placebo.

Reports of AEs between Vinh Wellness Collagen and placebo groups were similar in number when separated by system organ class category, indicating no significant difference between the two groups in terms of AEs experienced. All AEs were resolved by study end.

Efficacy

1) Overall Assessment via VAS

There were no significant differences between Vinh Wellness Collagen group and placebo in average skin quality VAS scores after the 12-week supplementation.

However, participants on Vinh Wellness Collagen reported greater percentage improvements over placebo in the overall (9%), elasticity (23%), hydration (14%), radiance (22%), firmness (25%), and wrinkle (15%) score.

Table 1: Comparison of change in Skin Quality VAS scores from baseline to week 12. Positive percentage indicates more improvement and negative percentage indicates less improvement in Vinh Wellness Collagen group compared to Placebo group.

	Change in VWC compared to Change in Placebo
Overall Feel of Skin	9%
Elasticity	23%
Hydration	14%
Radiance	22%
Firmness	25%
Wrinkle	15%

2) Wrinkle

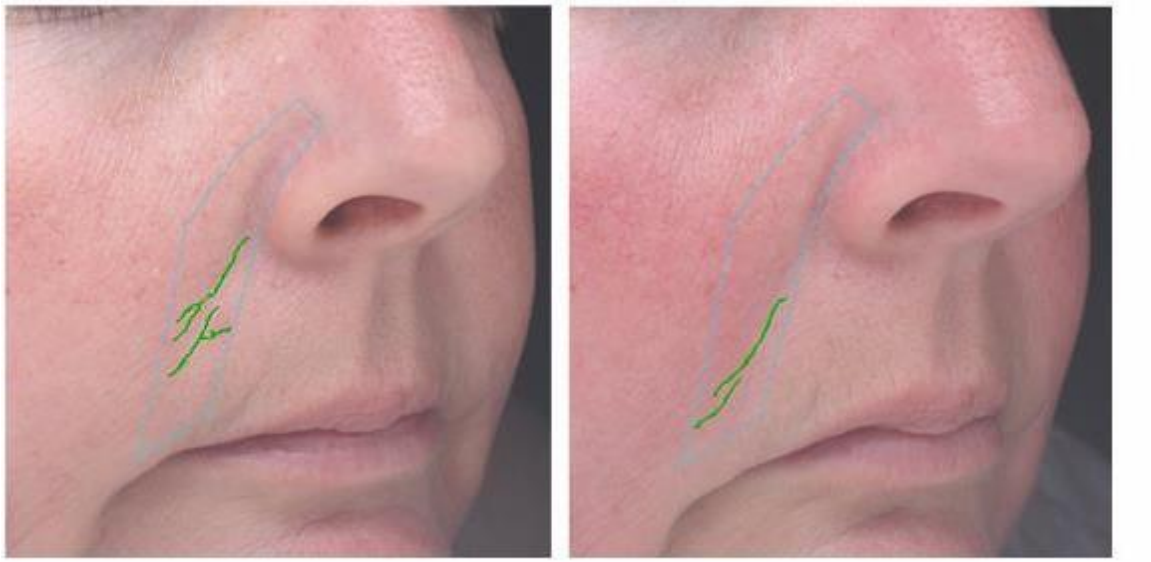
Participants supplemented with Vinh Wellness Collagen for 12 weeks showed significant improvement in absolute wrinkle score on the right side of their face compared to placebo. This change corresponded to a significant 35% reduction in wrinkle score without affecting the number of wrinkles.

Although there were no significant difference between groups, a significant 17% decrease in wrinkle score was seen in the Vinh Wellness Collagen group after the 12-week supplementation on the left side of the face.

It is interesting that the difference between treated and placebo groups is found to be significant for the right side of the face but not the left. This observation could be due to more photoaging on the left side. Both photoaging and melanoma are generally more prevalent on the left side of the face (Mac-Mary et al. 2010; Butler and Fosko 2010), indicating that the left side somehow ages more and faster than the right side. In the current study, despite the number of wrinkles at baseline was similar between the left and right side of the face for all participants, the absolute wrinkle score was approximately 20% higher on the left side compared to the right. The fact that the left side in our study population was more photoaged than the right is possibly the reason the efficacy of the product on the left side was detected but not significantly different compared to placebo. Longer treatment may show significant difference.

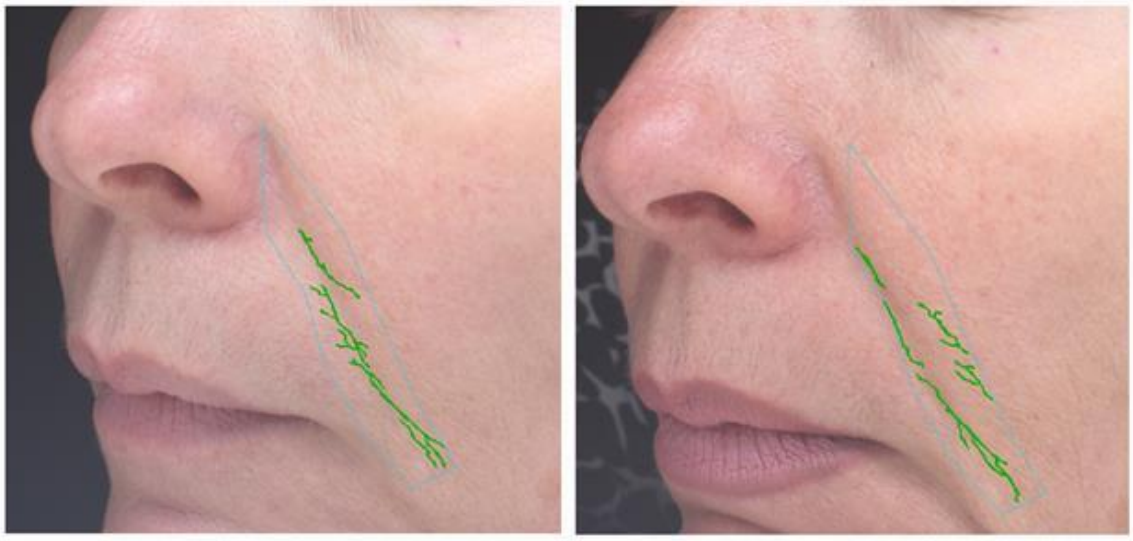
In previous research, following a 12-week supplementation with 10g fish collagen peptides, Asian women aged 59 years with a Fitzpatrick wrinkle score of 2-4 had a significant reduction in peri-orbital wrinkles by 10% as assessed by a VISIA (Bonnet, n.d). One reason for the larger improvement in the current study versus Bonnet (2017) may be that the concentration of anti-oxidants (glycine, proline and hydroxyproline which account for more than 50% of VWC) that positively affect wrinkles was higher in the current study.

Figure 2: A Typical Image Taken by the VISIA to Determine the Wrinkle Count and Wrinkle Feature Score for a Participant on Vinh Wellness Collagen at Baseline (Wrinkle Count = 2, Wrinkle Score = 34) and Day 60 (Wrinkle Count = 2, Wrinkle Score = 24)



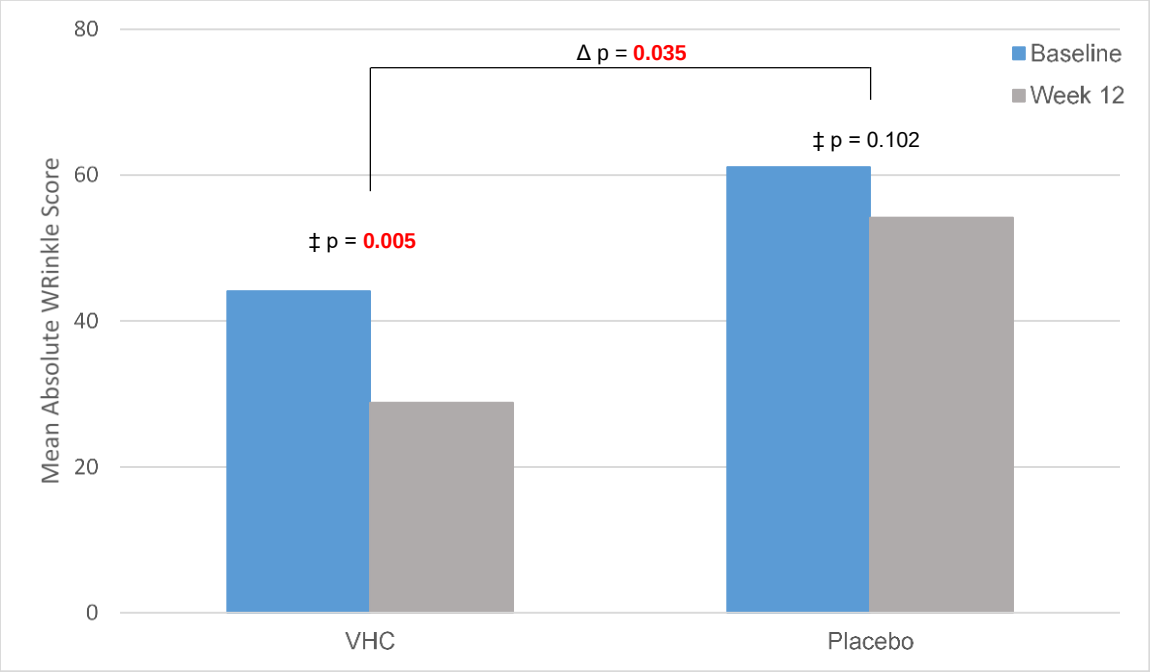
Baseline Day 60

Figure 3: A Typical Image Taken by the VISIA to Determine the Wrinkle Count and Wrinkle Feature Score for a Participant on Placebo at Baseline (Wrinkle Count = 4, Wrinkle Score = 56) and Day 60 (Wrinkle Count = 5, Wrinkle Score = 62)



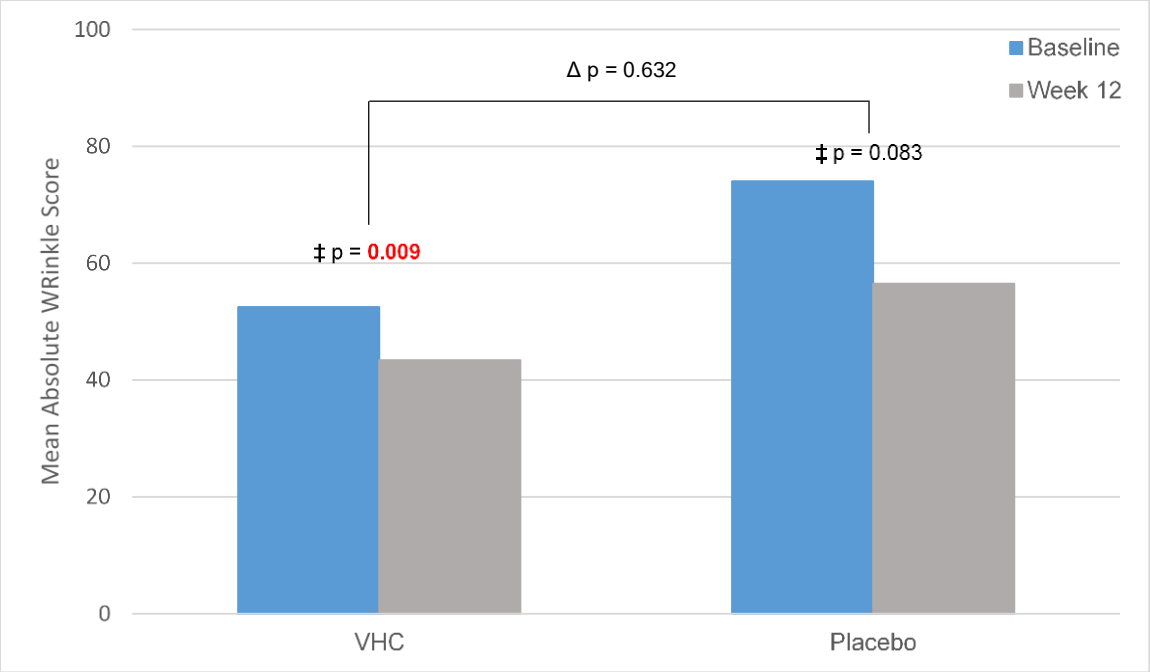
Baseline Day 60

Figure 4: Change in The Average Absolute Wrinkle Score for the Right Side of the Face of Participants in The PP Population (N = 36) as Assessed by the VISIA Skin Analysis. A 35% reduction in the Average Absolute Wrinkle score was seen in the Vinh Wellness Collagen group.



Δ Between-group comparisons were made using ANCOVA adjusting for baseline.
‡ Within-group comparisons were made using the non-parametric Wilcoxon signed-rank test.

Figure 5: Change in The Average Absolute Wrinkle Score for the Left Side of the Face of Participants in The PP Population (N = 36) as Assessed by the VISIA Skin Analysis. A 17% reduction in the Average Absolute Wrinkle score was seen in the Vinh Wellness Collagen group.



Δ Between-group comparisons were made using ANCOVA adjusting for baseline.
‡ Within-group comparisons were made using the non-parametric Wilcoxon signed-rank test.

3) Hydration

There were no significant differences in cheek skin hydration between or within Vinh Wellness Collagen and placebo groups as measured by the Corneometer. Although not statistically significant, participants supplemented with Vinh Wellness Collagen showed a 3% increase in cheek skin hydration whereas participants in placebo showed 5% decrease in skin hydration after 12 weeks.

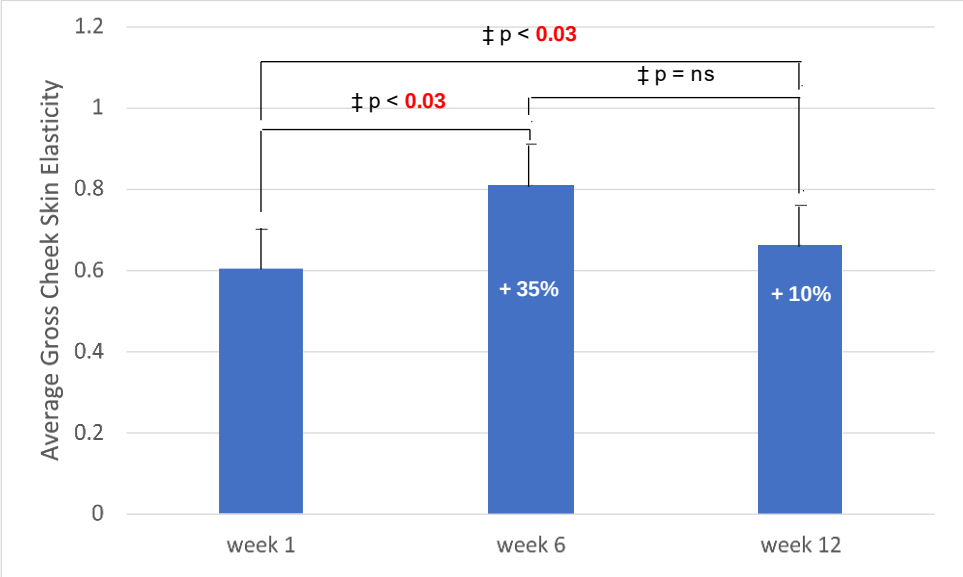
According to participants' evaluations as reported in the VAS results, skin moisture in the Vinh Wellness Collagen group was 14% higher than in the placebo group after 12 weeks of supplementation. Based on the results of the current study, it is reasonable to suggest that Vinh Wellness Collagen may be combined with other ingredients such as hyaluronic acid to provide faster results in skin hydration.

Previous studies have demonstrated improvements in skin elasticity and hydration following supplementation with hydrolyzed collagen (Proksch et al. 2014; Choi et al. 2014). Although there is convincing evidence for the beneficial effect of hydrolyzed collagen on skin from a preclinical perspective little is known about the actual clinical benefits (Tanaka et al. 2016; Proksch et al. 2014; Matsuda et al. 2006). This study suggests the possibility of using Vinh Wellness Collagen for improving skin elasticity and hydration.

4) Elasticity – Sub-Group Analysis on Participants 45-54 Years of Age

Cheek skin elasticity was significantly improved by 35% within the first 6 weeks of supplementation with Vinh Wellness Collagen in participants 45-54 years of age. The effect seems to level with no significant difference between week 6 and week 12. Overall, cheek skin elasticity was significantly improved by 10% from baseline to end of study in these participants.

Figure 6: Gross Cheek Skin Elasticity (R2) after supplementation with Vinh Wellness Collagen in participants 45-54 Years of age (N = 12), assessed by the Cutometer. Higher value indicates more elastic skin.



‡ Within-group comparisons were made using the non-parametric Wilcoxon signed-rank test.

References

Bonnet, Christine. n.d. “Introduction to Naticol® Marine Collagen Peptides for Anti-Aging and Overview of Clinical Studies.” The Scoular Company.

Butler, Susan T., and Scott W. Fosko. 2010. “Increased Prevalence of Left-Sided Skin Cancers.” *Journal of the American Academy of Dermatology* 63 (6): 1006–10. https://doi.org/10.1016/j.jaad.2009.11.032.

Choi, Sun Young, Eun Jung Ko, Yong Hee Lee, Byung Gyu Kim, Hyun Jung Shin, Dae Bang Seo, Sang Jun Lee, Beom Joon Kim, and Myeung Nam Kim. 2014. “Effects of Collagen Tripeptide Supplement on Skin Properties: A Prospective, Randomized, Controlled Study.” *Journal of Cosmetic and Laser Therapy: Official Publication of the European Society for Laser Dermatology* 16 (3): 132–37. https://doi.org/10.3109/14764172.2013.854119.

Mac-Mary, Sophie, Jean-Marie Sainthillier, Adeline Jeudy, Christelle Sladen, Cara Williams, Mike Bell, and Philippe Humbert. 2010. “Assessment of Cumulative Exposure to UVA through the Study of Asymmetrical Facial Skin Aging.” *Clinical Interventions in Aging* 5: 277–84.

Matsuda, Naoya, Yoh-ichi Koyama, Yoshinao Hosaka, Hiromi Ueda, Takafumi Watanabe, Takayuki Araya, Shinkichi Irie, and Kazushige Takehana. 2006. “Effects of Ingestion of Collagen Peptide on Collagen Fibrils and Glycosaminoglycans in the Dermis.” *Journal of Nutritional Science and Vitaminology* 52 (3): 211–15.

Proksch, Ehrhard, Dörte Segger, Joachim Degwert, Michael Schunck, Vivian Zague, and Steffen Oesser. 2014. “Oral Supplementation of Specific Collagen Peptides Has Beneficial Effects on Human Skin Physiology: A Double-Blind, Placebo-Controlled Study.” *Skin Pharmacology and Physiology* 27 (1): 47–55. https://doi.org/10.1159/000351376.

Tanaka, Miyuki, Yuki Yamamoto, Eriko Misawa, Kazumi Nabeshima, Marie Saito, Koji Yamauchi, Fumiaki Abe, and Fukumi Furukawa. 2016. “Effects of Aloe Sterol Supplementation on Skin Elasticity, Hydration, and Collagen Score: A 12-Week Double-Blind, Randomized, Controlled Trial.” *Skin Pharmacology and Physiology* 29 (6): 309–17. https://doi.org/10.1159/000454718.

Signatories

The current randomized, double-blind, placebo-controlled study was designed per ICH guidelines and met the regulatory requirements for the investigation of a dietary supplement in healthy individuals. The protocol was written per ICH guidelines and incorporated a sample calculation, a statistical plan, and inclusion and exclusion criteria ensuring the enrolment of healthy participants and detailed all study visits and procedures at the outset. Regulatory and ethics approvals were obtained, and all participants signed informed consent prior to any procedures being conducted. GCP guidelines were adhered to during the conduct of the study. Study personnel including statisticians remained blinded until all study related procedures were completed, the data analyzed, and the database was locked.

Independent Ethics Committee (IEC) or Institutional Review Board

This study was reviewed by the Natural Health Product Directorate (NHPD), Health Canada and the Institutional Review Board Services (IRB Service). Notice of authorization was granted on June 13th, 2016 by the NHPD, Ottawa, Ontario and unconditional approval was granted on June 28th, 2016 by the IRB Services, Aurora, Ontario.

Three amendments were made to the protocol dated June 21st, 2016 and approved by IRB. The last amendment was approved on March 31st, 2017.

Ethical Conduct of the Study

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and its subsequent amendments.

Participant Information and Consent

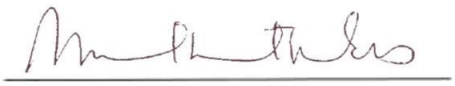
Informed consent was obtained from each participant at the Screening visit (Visit 1) prior to any study-related activities being performed.

Investigators and Study Administrative Structure

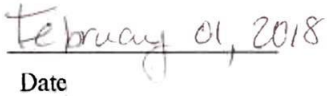
The clinical trial was conducted at KGK Science Inc. (London, Ontario, Canada), under the supervision of the Medical Director/ Qualified Investigator, Tetyana Pelipyagina, M.D. Statistical analysis was conducted by Xiaojian Yang, Ph.D., and the report was authored by Malkanthi Evans, Ph.D.

Signature

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study

Scientific Director: 

Malkanthi Evans, Ph.D.
Scientific Director
KGK Science Inc.



Date