AETHERN®

advanced skin beauty program

Clinical Efficacy Study Report

Conducted by:

DERMATOLOGY CONSULTING SERVICES
2444 North Main Street
High Point, NC 27262
(USA)

And led by:

Dr. Zoe Diana Draelos, MD, PA

Overview

In order to evaluate the efficacy of **AETHERN**® advanced skin beauty program, we commissioned a clinical study of a group of 70 women between 40 and 59, with mild to moderate photoaging.

The objective of this research was to determine the ability of a nutritional supplement to improve the appearance of skin health as characterized by improved skin Hydration, Firmness, Radiance and UV Protection.

Methodology

Over the 12-weeks period, women took a daily dose of **AETHERN**® advanced skin beauty program.

Clinical Efficacy Study Report

General Results After 12 Weeks

Aethern Report

April 25, 2017

The Ability of a Novel Nutritional Supplement to Improve the Appearance of Skin Health

STUDY NUMBER: DCS-71-16

INVESTIGATOR: ZOE DIANA DRAELOS, M.D.

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SPONSOR: Aethern

PRODUCT: Aethern Nutritional Supplement

PROTOCOL NUMBER: DCS-71-16

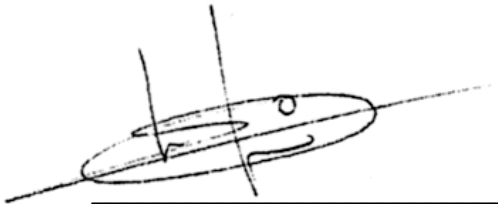
PROTOCOL SYNOPSIS DATE: September 16, 2016

PROTOCOL DATE: September 30, 2016

MARKETING REPORT DATE: April 25, 2017

STUDY TITLE: The Ability of a Novel Nutritional Supplement to Improve the Appearance of Skin Health

Signatures of the noted individuals ensure that all designated persons have agreed this version of the marketing report is final.



05-08-2017

Representative
Aethern
Mr. Adil Falco
Biogenic Pharma, sl. - CEO

Date

05/08/17

Zoe Diana Draelos, M.D.
Primary Investigator
Dermatology Consulting Services

Date

1. PROTOCOL SYNOPSIS

Title of Study:	The Ability of a Novel Nutritional Supplement to Improve the Appearance of Skin Health
Study Period:	12 weeks
Test Product:	Aethern nutritional supplement (25ml) consumed once daily.
Control Product:	Subjects provided with a control product (25ml) for consumption once daily composed of fructose and cherry flavoring.
Objective:	The objective of this research was to determine the ability of a nutritional supplement to improve the appearance of skin health as characterized by improved skin hydration, firmness, and radiance.
Design:	This research was a double-blind placebo controlled parallel group study design to evaluate the effects of a once daily nutritional supplement on skin hydration, firmness, and radiance. Eligible subjects who passed a phone screening questionnaire presented to the research facility for inclusion/exclusion evaluation following completion of an IRB approved informed consent. Half of the subjects were randomized to receive the study supplement while the remainder of the subjects received the control product. The research coordinator performed all dispensing and maintained the blind until the study was completed. Every effort was made to balance the two groups in terms of subject demographics. Enrolled subjects were assessed at baseline, 4 weeks, 8 weeks, and 12 weeks. The same assessments were performed at each visit to the research center. Assessments were performed on the face and on a template identified target site on the inner right and left arms. The template was used to identify a consistent location for inner arm measurement. Dermatologist investigator and subject questionnaires were completed assessing skin appearance attributes for both the face and the sun-protected inner arm. Photography of the front, right, and left face was performed. Subjects underwent several noninvasive assessments including corneometry to evaluate skin hydration and elastometry to assess skin firmness of both the face and the right/left inner arm. Subjects were dispensed either the study supplement or the control at each visit and a compliance diary. The research coordinator evaluated the diaries for proper completion and addressed any compliance issues. At the 12 week study completion, all study materials were collected from the subjects and they were released from further study participation.
Study Population:	70 Female subjects 40-59 years of age with mild to moderate photoaging
Number of	70 qualified subjects (35 subjects consumed the study product, 35 subjects

Subjects:	consumed the control product based on a computer generated randomization scheme maintained by the research coordinator)
Inclusion Criteria:	The following items represented the inclusion criteria: 1. Subjects must be female 40-59 years of age with mild to moderate photoaging of Fitzpatrick skin types I-IV. 2. Subjects must possess no known medical conditions that, in the investigator's opinion, may interfere with study participation. 3. Subjects must possess normal skin on the face and body. 4. Women of childbearing potential must be willing to use a form of birth control during the study. For the purpose of this study, the following are considered acceptable methods of birth control: oral contraceptives, Norplant®, Depo-Provera®, double barrier methods (e.g., condom and spermacide) and abstinence. 5. Subjects must provide written informed consent. 6. Subjects must be willing to comply with the study design and procedures.
Exclusion Criteria:	The following items represented the exclusion criteria: 1. Any dermatological disorder, which in the investigator's opinion, may interfere with the accurate evaluation of the subject's skin characteristics. 2. Subjects who possess gluten intolerance. 3. Subjects must maintain consistent dietary habits before and during the entire study. 4. Subjects who are planning to initiate any new or changed hormonal treatments during the study and three months prior to the study. 5. Subjects who are pregnant, breast feeding or planning a pregnancy. 6. Subjects who receive extensive sun exposure just before and during the entire research study. 7. Subjects with clinically significant unstable medical disorders. 8. Subjects who are unwilling or unable to comply with the requirements of the protocol. 9. Subjects who have history of a psychological illness or condition that would interfere with their ability to understand and follow the requirements of the study.
Endpoint:	<u>Primary Efficacy Endpoint:</u> The primary efficacy endpoint was the investigator assessed superior skin hydration of the face and body induced by the dietary supplement as compared to the control supplement. <u>Secondary Efficacy Endpoint:</u> The secondary efficacy endpoint was the investigator assessed superior skin firmness of the face and body induced by the dietary supplement as compared to the control supplement. <u>Tertiary Efficacy Endpoint:</u>

	The tertiary efficacy endpoint was the investigator assessed superior skin radiance of the face and body induced by the dietary supplement as compared to the control supplement. Tolerability Endpoint: The tolerability endpoint was the subject assessed gastrointestinal issues associated with the study supplement.
Measures:	All assessments occurred at baseline, week 4, week 8, and week 12. Investigator Efficacy Assessments: The dermatologist investigator assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance. Subject Efficacy Assessments: The subjects assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance. Subject Tolerability Assessments: The subjects were asked about any gastrointestinal issues associated with the consumption of the study products. Photography: high quality jpeg photographs were taken of the front, right, and left face at rest with the eyes closed, hair pulled back with a black head band, and clothing draped with a black cloth on a black background. Subjects were placed in a Canfield 3 point head mount with Canfield designed Nikon camera and flash system. Noninvasive Assessments: Corneometry: A pin probe corneometer (Cortex Technologies, Denmark) was used to obtain an instantaneous reading of the left face at the zygomatic arch and left inner templated forearm. Elastometry: An elastometer (Cortex Technologies, Denmark) was used to assess skin elasticity on the right zygomatic arch and the right inner templated forearm.
Statistical Methods:	A two-tailed Mann Whitney t test was used to analyze the nonparametric data sets (investigator efficacy assessments for face and body, subject efficacy and tolerability assessments for face and body) with significance set at $p<0.05$. The active and control study data was analyzed longitudinally for an intragroup analysis and as change from baseline/direct comparison for intergroup comparisons. The ordinal parametric noninvasive data (corneometry, elastometry) was analyzed using a Student t test with significance set at $p<0.05$.

2. STUDY VISIT SCHEDULE

Procedures	Visit 1 BL	Visit 2 Wk4	Visit 3 Wk8	Visit 4 Wk12
Consent, exclusion and inclusion criteria	X			
Brief medical history	X			
Investigator efficacy assessment (face and inner arm)	X	X	X	X
Subject assessment for tolerability and efficacy (face and inner arm)	X	X	X	X
Photography (face only)	X	X	X	X
Noninvasive Assessments: Corneometry, Elastometry (face and body)	X	X	X	X
Study Product Dispensing	X	X	X	
Diary Assessment		X	X	X
Study Product Accountability		X	X	X
Release from Study Participation				X

3. INTRODUCTION

Overall body health is readily reflected in the skin. Thus, nutrition is an important part of skin appearance as characterized by skin hydration, firmness, and radiance. Skin hydration is an assessment of the water content of the skin, which is optimal at approximately 30%. Water is the plasticizer of the skin allowing the skin to appear smooth and feel soft. Dehydrated skin is scaly, rough, and dull. All skin water is derived from oral consumption and maintained in the skin through naturally occurring humectants, primarily glycosaminoglycans (GAGs) such as hyaluronic acid. Firmness is an indirect consequence of proper skin hydration as water improves skin firmness minimizing wrinkling and folding of the skin. Finally, skin that is well hydrated and firm is also radiant, a measure of light reflection from a smooth skin surface. Radiant skin is characterized by a healthy glow representing light entering the observer's eye that is reflected from an even skin surface.

This research examined a dietary supplement designed to improve skin health by increasing hydration, enhancing firmness, and improving radiance.

4. STUDY OBJECTIVE

The objective of this research was to determine the ability of a nutritional supplement to improve the appearance of skin health as characterized by improved skin hydration, firmness, and radiance.

5. STUDY DESIGN OVERVIEW

This research was a double-blind placebo controlled parallel group study design to evaluate the effects of a once daily nutritional supplement on skin hydration, firmness, and radiance. Eligible subjects who passed a phone screening questionnaire presented to the research facility for inclusion/exclusion evaluation following completion of an IRB approved informed consent. Half of the subjects were randomized to receive the study supplement while the remainder of the subjects received the control product. The research coordinator performed all dispensing and maintained the blind until the study was completed. Every effort was made to balance the two groups in terms of subject demographics. Enrolled subjects were assessed at baseline, 4 weeks, 8 weeks, and 12 weeks. The same assessments were performed at each visit to the research center. Assessments were performed on the face and on a template identified target site on the inner right and left arms. The template was used to identify a consistent location for inner arm measurement. Dermatologist investigator and subject questionnaires were completed assessing skin appearance attributes for both the face and the sun-protected inner arm. Photography of the front, right, and left face was performed. Subjects underwent several noninvasive assessments including corneometry to evaluate skin hydration and elastometry to assess skin firmness of both the face

and the right/left inner arm. Subjects were dispensed either the study supplement or the control at each visit and a compliance diary. The research coordinator evaluated the diaries for proper completion and addressed any compliance issues. At the 12 week study completion, all study materials were collected from the subjects and they were released from further study participation.

6. STUDY POPULATION

6.1 NUMBER OF SUBJECTS

70 Female subjects 40-59 years of age Fitzpatrick skin types I-IV with mild to moderate photoaging

6.2 INCLUSION CRITERIA

The following items represented the inclusion criteria:

1. Subjects must be female 40-59 years of age with mild to moderate photoaging of Fitzpatrick skin types I-IV.
2. Subjects must possess no known medical conditions that, in the investigator's opinion, may interfere with study participation.
3. Subjects must possess normal skin on the face and body.
4. Women of childbearing potential must be willing to use a form of birth control during the study. For the purpose of this study, the following are considered acceptable methods of birth control: oral contraceptives, Norplant®, Depo-Provera®, double barrier methods (e.g., condom and spermacide) and abstinence.
5. Subjects must provide written informed consent.
6. Subjects must be willing to comply with the study design and procedures.

6.3 EXCLUSION CRITERIA

The following items represented the exclusion criteria:

1. Any dermatological disorder, which in the investigator's opinion, may interfere with the accurate evaluation of the subject's skin characteristics.
2. Subjects who possess gluten intolerance.
3. Subjects must maintain consistent dietary habits before and during the entire study.
4. Subjects who are planning to initiate any new or changed hormonal treatments during the study and three months prior to the study.
5. Subjects who are pregnant, breast feeding or planning a pregnancy.
6. Subjects who receive extensive sun exposure just before and during the entire research study.
7. Subjects with clinically significant unstable medical disorders.
8. Subjects who are unwilling or unable to comply with the requirements of the protocol.
9. Subjects who have history of a psychological illness or condition that would interfere with their ability to understand and follow the requirements of the study.

6.4 CONCOMITANT MEDICATIONS & RESTRICTIONS

There were no medication restrictions, however subjects did not change any medications for the duration of the study.

7. CONDUCT OF STUDY: METHODS AND PROCEDURES

7.1 ENROLLMENT PROCEDURES

7.1.1 INFORMED CONSENT

A signed Institutional Review Board (IRB) approved informed consent form was obtained from each subject before any study procedures were performed. No study related procedures or activities were performed until each subject was fully informed and the consent form was signed and dated.

7.1.2 MEDICAL HISTORY

An abbreviated medical history including current medications was recorded.

7.1.3 DERMATOLOGIC EXAMINATION

A dermatologic examination was performed. Patients had no skin conditions, which interfered with the study results in the opinion of the dermatologist investigator.

7.1.4 SCREENING PROCEDURES

Subjects were screened for the presence of mild to moderate photoaging.

7.1.5 STUDY ENROLLMENT PROCEDURES

The subjects were screened for the inclusion and exclusion criteria prior to study enrollment. Only subjects who met the requirements, signed an informed consent, and gave a medical history were entered into the study. All other subjects were considered screening failures.

7.1.6 STUDY MATERIALS

All study subjects received the currently marketed study supplement or a placebo. The placebo consisted of cherry flavored water sweetened with fructose.

7.2 STUDY CONDUCT PROCEDURES

This section outlines the study procedures that were conducted at each visit.

7.2.1 BASELINE

Eligible subjects who have passed a phone screening questionnaire presented to the research facility for inclusion/exclusion evaluation following completion of an IRB approved informed consent. Half of the subjects were randomized to receive the study supplement while the remainder of the subjects received the control product. The research coordinator performed all dispensing and maintained the blind until the study was completed. Every effort was made to balance the two groups in terms of subject demographics.

Assessments were performed on the entire face and on a template identified target site on the inner right and left arms. The template was used to identify a consistent location for inner arm noninvasive measurement. The following assessments were conducted at baseline:

Investigator Efficacy Assessments: The dermatologist investigator assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Efficacy Assessments: The subjects assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Tolerability Assessments: The subjects were queried for any underlying gastrointestinal issues that might be pre-existing.

Photography: High quality jpeg photographs were taken of the front, right, and left face at rest with the eyes closed, hair pulled back with a black headband, and clothing draped with a black cloth on a black background. Subjects were placed in a Canfield 3 point head mount with Canfield designed Nikon camera and flash system.

Noninvasive Assessments:
Corneometry: A pin probe corneometer (Cortex Technologies, Denmark) was used to obtain an instantaneous reading of the left face at the zygomatic arch and left inner templated forearm.
Elastometry: An elastometer (Cortex Technologies, Denmark) was used to assess skin elasticity on the right zygomatic arch and the right inner templated forearm.

Subjects were educated on how to properly consume their randomized study product and also received instructions on how to complete the compliance diary. All subjects were given a schedule of the return visit times and dates for the entire study, along with a reminder card for the next visit to the research center at week 4. Subjects received a reminder text for their visit at week 4 the evening prior to the scheduled visit to decrease subject dropout.

7.2.2 WEEK 4

Subjects returned to the research center at week 4. They brought back their used supplement containers for inspection to be sure that compliance was maintained. In addition, the study diaries were inspected for proper completion and compliance. The following evaluations were completed on the entire face and on a template identified target site on the inner right and left arms:

Investigator Efficacy Assessments: The dermatologist investigator assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Efficacy Assessments: The subjects assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Tolerability Assessments: The subjects were asked about any gastrointestinal issues associated with the consumption of the study products.

Photography: High quality jpeg photographs were taken of the front, right, and left face at rest with the eyes closed, hair pulled back with a black headband, and clothing draped with a black cloth on a black background. Subjects were placed in a Canfield 3 point head mount with Canfield designed Nikon camera and flash system.

Noninvasive Assessments:
Corneometry: A pin probe corneometer (Cortex Technologies, Denmark) was used to obtain an instantaneous reading of the left face at the zygomatic arch and left inner templated forearm.
Elastometry: An elastometer (Cortex Technologies, Denmark) was used to assess skin elasticity on the right zygomatic arch and the right inner templated forearm.

Subjects were redispensed enough study product for the next 4 weeks until their next visit to the research center. In addition, they received a reminder card for their next visit to the research center at week 8. Subjects received a reminder text for their visit at week 8 the evening prior to the scheduled visit to decrease subject dropout.

7.2.3 WEEK 8

Subjects returned to the research center at week 8. They brought back their used supplement containers for inspection to be sure that compliance was maintained. In addition, the study diaries were inspected for proper completion and

compliance. The following evaluations were completed on the entire face and on a template identified target site on the inner right and left arms:

Investigator Efficacy Assessments: The dermatologist investigator assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Efficacy Assessments: The subjects assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Tolerability Assessments: The subjects were asked about any gastrointestinal issues associated with the consumption of the study products.

Photography: High quality jpeg photographs were taken of the front, right, and left face at rest with the eyes closed, hair pulled back with a black headband, and clothing draped with a black cloth on a black background. Subjects were placed in a Canfield 3 point head mount with Canfield designed Nikon camera and flash system.

Noninvasive Assessments:
Corneometry: A pin probe corneometer (Cortex Technologies, Denmark) was used to obtain an instantaneous reading of the left face at the zygomatic arch and left inner templated forearm.
Elastometry: An elastometer (Cortex Technologies, Denmark) was used to assess skin elasticity on the right zygomatic arch and the right inner templated forearm.

Subjects were redispensed enough study product for the next 4 weeks until their next visit to the research center. In addition, they received a reminder card for their next visit to the research center at week 12. Subjects received a reminder text for their visit at week 12 the evening prior to the scheduled visit to decrease subject dropout.

7.2.4 WEEK 12

Subjects returned to the research center at week 12. They brought back their used supplement containers for inspection to be sure that compliance was maintained. In addition, the study diaries were inspected for proper completion and compliance. The following evaluations were completed on the entire face and on a template identified target site on the inner right and left arms:

Investigator Efficacy Assessments: The dermatologist investigator assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Efficacy Assessments: The subjects assessed the skin on the face and the sun-protected inner left arm separately on a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe. The following attributes were assessed: hydration, firmness, radiance.

Subject Tolerability Assessments: The subjects were asked about any gastrointestinal issues associated with the consumption of the study products.

Photography: High quality jpeg photographs was taken of the front, right, and left face at rest with the eyes closed, hair pulled back with a black headband, and clothing draped with a black cloth on a black background. Subjects were placed in a Canfield 3 point head mount with Canfield designed Nikon camera and flash system.

Noninvasive Assessments:
Corneometry: A pin probe corneometer (Cortex Technologies, Denmark) was used to obtain an instantaneous reading of the left face at the zygomatic arch and left inner templated forearm.
Elastometry: An elastometer (Cortex Technologies, Denmark) was used to assess skin elasticity on the right zygomatic arch and the right inner templated forearm.

All subjects discontinued study participation at this time and all study materials and diaries were collected.

8. SUBJECT COMPLIANCE

Subject compliance was determined by examining the empty supplement containers that were returned to the study center. In addition, subjects maintained compliance diaries.

9. FINAL SUBJECT STATUS

A study termination form was completed for each study subject who completed the informed consent process. 68/70 subjects completed the study. The study demographics are listed in the table below:

Demographic Log				
Subject #	Subject Initials	Age	Gender	Race
1	SPC	47	F	C
2	HRL	40	F	C
3	AMI	40	F	C
4	ALB	42	F	C
5	JYG	55	F	C
6	DPJ	57	F	C
7	APH	58	F	C
8	CAS	53	F	C
9	SLM	50	F	C
10	DSW	53	F	C
11	LLV	54	F	C
12	GAB	49	F	C
13	JAM	54	F	C
14	MLC	49	F	C
15	BLH	54	F	C
16	LWC	55	F	C
17	PJO	55	F	C
18	DER	54	F	C
19	JEW	47	F	C
20	KLH	59	F	C
21	ACE	44	F	C
22	SCV	46	F	C
23	MCR	56	F	C
24	DRB	59	F	C
25	RJS	55	F	C

Demographic Log				
Subject #	Subject Initials	Age	Gender	Race
26	KAB	53	F	C
27	ABH	47	F	C
28	SGW	55	F	C
29	DAN	53	F	C
30	JAH	52	F	C
31	TSA	55	F	C
32	TMB	57	F	C
33	MRW	52	F	C
34	TTE	54	F	C
35	LSW	50	F	C
36	SEM	56	F	C
37	STM	58	F	C
38	SKS	55	F	C
39	EAD	56	F	C
40	KJM	53	F	C
41	RRS	52	F	C
42	DMR	57	F	C
43	TLS	57	F	C
44	ASW	49	F	C
45	KBM	54	F	C
46	RMR	54	F	C
47	ASP	56	F	C
48	BAC	50	F	C
49	LLM	57	F	C
50	DRB	54	F	C

Demographic Log				
Subject #	Subject Initials	Age	Gender	Race
51	KEM	55	F	C
52	SBC	52	F	C
53	MLC	51	F	C
54	DYT	56	F	C
55	SAK	47	F	C
56	PHC	40	F	C
57	CSB	48	F	C
58	DPC	54	F	C
59	JMC	55	F	C
60	LWK	52	F	C
61	CLC	53	F	C
62	JLB	48	F	C
63	CNJ	50	F	C
64	LLN	53	F	C
65	LWD	49	F	C
66	L-G	55	F	C
67	LAF	54	F	C
68	CKT	49	F	C
69	MLW	46	F	C
70	JML	40	F	C

Demographic Log Key	
	Race
AA	African American
BR	Bi-Racial
C	Caucasian
H	Hispanic
A	Asian
I	Indian
O	Other

10. STUDY PRODUCTS

10.1 DOSAGE AND FORMULATIONS

The subjects received a currently marketed liquid supplement or a placebo consisting of fructose and cherry flavoring. Either the supplement or the placebo was consumed once daily.

10.2 PRECAUTIONS

The study supplement or placebos were consumed once daily. Subjects were given a list of the study supplement and placebo contents. Subjects who were allergic to any of the ingredients were not enrolled in the research.

10.3 STUDY PRODUCT ADMINISTRATION

The study supplement or placebo was consumed once daily for 12 weeks.

10.4 PACKAGING, LABELING, DISTRIBUTION

The study supplement was dispensed to the subjects in the packaging provided by the sponsor.

10.5 STORAGE AND ACCOUNTABILITY OF STUDY PRODUCT

The study supplements were stored at room temperature in a locked, limited access area at the study site. Access to the study devices was limited to the investigator and staff members designated to dispense study medication. A study product log was used to record the use of all study product. The subject

number/initials and the initials and date of the person using the study product was documented.

11. ADVERSE EVENTS AND ADVERSE EXPERIENCES

No adverse events occurred during the administration of the study. Several subjects noted burping, indigestion, and flatulence related to consumption of the study product. This data is discussed under the results tolerability section of this report as these were expected adverse experiences.

12. STATISTICAL METHODS

A Mann-Whitney test was used to analyze the investigator and subject ordinal efficacy data and investigator tolerability data. A Student t test was used to analyze the noninvasive assessments. Data was analyzed in an intergroup fashion comparing the nutritional supplement to the flavored sweetened water placebo.

12.1 SAMPLE SIZE RATIONALE

The sample size of 70 subjects, intended to complete 60 subjects, was chosen by the sponsor based on the number of subjects required to reach statistical significance in this placebo controlled trial. 68 subjects completed the research study.

12.2 SIGNIFICANCE LEVEL

Significance was defined at the p=0.05 or less level.

12.3 SAFETY ASSESSMENT

No safety issues arose during the conduct of the research.

13. RESULTS

The results for the study are presented in the attached Excel data tables.
Table 1: Corneometry Face and Arm
Table 2: Elastometry Face and Arm
Table 3: Investigator Efficacy Assessment Arm
Table 4: Investigator Efficacy Assessment Face
Table 5: Investigator Tolerability Assessment
Table 6: Subject Efficacy Assessment Arm
Table 7: Subject Efficacy Assessment Face
Table 8: Subject Tolerability Assessment

The data was analyzed using three different statistical techniques. Two intergroup comparisons (direct comparison and difference from baseline) were used and one

intragroup comparison (longitudinal) was used. The direct comparison analysis compared the raw ordinal data collected at each time point to baseline. The difference from baseline analysis subtracted the ordinal data at each time point from the baseline to evaluate the change over time. Finally, the longitudinal analysis compared the ordinal rating for each arm of the study, placebo or active, to baseline.

14. DISCUSSION

The results are discussed separately for each data set.

Table 1: Corneometry Face and Arm
Corneometry measured the amount of water in the skin of the face and arm. The reading was taken with a pin probe that measured the amount of electricity conducted through the skin as a result of water content. Readings were taken from the left templated inner left arm and the left zygomatic arch. A higher number is indicative of superior skin hydration. The longitudinal analysis demonstrated some statistically significant differences. The placebo showed a statistically significant change of 20% improvement in arm hydration at week 4 ($p=0.028$) and week 8 ($p<0.001$). The same analysis also showed a statistically significant improvement with the nutritional supplement in face hydration of 23% at week 8 ($p=0.002$). There was an increase in arm hydration with the nutritional supplement at week 8 of 53% ($p<0.001$).

Table 2: Elastometry Face and Arm
Elastometry was performed from the right zygomatic arch, which is the upper right cheek bone, and the right templated sun protected inner forearm. The skin elasticity machine used negative pressure to pull the skin into a suction cup following relaxation to evaluate the effect of the nutritional supplement on skin elasticity and firmness. The longitudinal assessment examined intragroup changes over time. In the supplement group, the face elasticity increased 14% at week 4 ($p=0.016$), 20% at week 8 ($p=0.001$), and 29% at week 12 ($p<0.001$). The arm elasticity increased 7% at week 4 ($p=0.020$) and 8% at week 8 ($p=0.006$).

Table 3: Investigator Efficacy Assessment Arm
The investigator assessed hydration, firmness, and radiance on the inner arms at baseline, week 4, week 8, and week 12 in both the active supplement and placebo groups. At week 8, there was a statistically significant improvement hydration ($p=0.011$), firmness ($p=0.004$), and radiance ($p<0.001$) with the direct comparison in the group that consumed the active nutritional supplement over the group that consumed the placebo as assessed by the investigator. This improvement continued into week 12 in terms of hydration ($p=0.001$), firmness ($p=0.003$), and radiance ($p<0.001$) also with the direct comparison method.

These same findings were also present with the difference from baseline assessment, which is the more accurate evaluation given the statistical difference between the active nutritional supplement and the placebo group at baseline in terms of radiance. The difference from baseline analysis showed statistically significant improvements with the

active nutritional supplement over the placebo in terms of hydration (p=0.035), firmness (p<0.001), and radiance (p=0.003). These benefits continued into week 12 with statistically significant improvement in hydration (p=0.004), firmness (p<0.001), and radiance (p<0.001).

The longitudinal assessment showed a 21% improvement in arm hydration (p=0.001), 22% improvement in arm firmness (p=0.001), and 28% improvement in arm radiance (p<0.001) after 12 weeks of taking the nutritional supplement. Improvement was seen as early as week 8, with a 12% improvement in arm hydration (p=0.025), 17% improvement in arm firmness (p=0.005), and 13% improvement in arm radiance (p=0.009).

Table 4: Investigator Efficacy Assessment Face
Separate assessments were made for the face. The difference from baseline showed a statistically significant improvement in firmness (p=0.037) in the group taking the active nutritional supplement over the placebo group. This improvement continued into week 8 with statistically significant improvement in hydration (p=0.008) and firmness (p<0.001) in the active supplement group. By week 12, the active supplement group showed improvement in hydration (p=0.013), firmness (p<0.001), and radiance (p=0.031). This translated into a 19% improvement in hydration, 22% improvement in firmness, and 23% improvement in radiance after 12 weeks of consuming the active nutritional supplement.

Table 5: Investigator Tolerability Assessment
There was a statistically significant increase in flatulence (p=0.018), burping (p=0.018), and indigestion (p=0.041) at week 12 with the direct comparison analysis in the active supplement group over the placebo group. These same findings were found with the difference from baseline analysis.

Table 6: Subject Efficacy Assessment Arm
The subjects assessed the hydration, firmness, and radiance of their arm skin. The direct comparison analysis revealed a statistically significant improvement in skin hydration with the active supplement at week 8 (p=0.020), which did not continue into week 12. However, firmness became statistically significant at week 12 (p=0.008). The longitudinal analysis showed a statistically significant improvement in hydration, firmness, and radiance at weeks 8 and 12 with the active supplement that was not seen with the placebo. With the difference from baseline analysis, a statistically significant improvement in firmness was noted at week 12 (p=0.009) in the active supplement group over the placebo group. This might indicate that the study was underpowered.

Table 7: Subject Efficacy Assessment Face
The subjects also assessed the hydration, firmness, and radiance of their facial skin. There was a statistically significant improvement in firmness at weeks 4 (p=0.041), 8 (p=0013), and 12 (p=0.040) and a statistically significant improvement in radiance at week 8 (p=0.005) with the active group over the placebo group.

Table 8: Subject Tolerability Assessment
No tolerability issues arose based on subject evaluations of flatulence, burping, or indigestion. Thus, the subjects felt the nutritional supplement was well tolerated.

15. SUMMARY

15.1 PRIMARY EFFICACY ENDPOINT

The primary efficacy endpoint was the investigator assessed superior skin hydration of the face and body induced by the dietary supplement as compared to the control supplement. The primary efficacy endpoint was met.

15.2 SECONDARY EFFICACY ENDPOINT

The secondary efficacy endpoint was the investigator assessed superior skin firmness of the face and body induced by the dietary supplement as compared to the control supplement. The secondary efficacy endpoint was met.

15.3 TERTIARY EFFICACY ENDPOINT

The tertiary efficacy endpoint was the investigator assessed superior skin radiance of the face and body induced by the dietary supplement as compared to the control supplement. The tertiary efficacy endpoint was met.

15.4 TOLERABILITY ENDPOINT

The tolerability endpoint was the subject assessed gastrointestinal issues associated with the study supplement. The tolerability endpoint was met.