Technical Summary of Cynatine® HNS Clinical Trial

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February 2020

1. Evaluation of Cynatine on Hair
   - This study looks at the effects of Cynatine on Hair, Skin and Nails
   - The section on hair analyzes 5 different tests to evaluate the effect on hair

a. Hair Pull Test
   -The Hair Pull Test evaluates hair loss from every day activity such as washing and brushing
   - Gentle traction is provided to a total of approximately 60 hairs in three areas of the scalp and the total number of hairs extracted is counted
   - Healthy hairs in the anagen phase should remained rooted, while hairs in the telogen phase should be extracted

Table 1. Analyses (Hair- Pull Test)

Pull Test Score	Study Group				
	Placebo		Cynatine® HNS		
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	p-value between groups
Baseline	13.0 ± 1.9		12.9 ± 1.8		
Day 30	11.9 ± 1.9		9.8 ± 1.3		
Day 60	11.6 ± 1.3		7.2 ± 1.2		
Day 90	10.9 ± 1.4		6.9 ± 0.8		
Change to Baseline:					
Day 30	-1.1 (-7.6%)	p < 0.001	-3.1 (-24.5%)	p < 0.001	p < 0.001
Day 60	-1.4 (-9.9%)	p < 0.001	-5.7 (-44.3%)	p < 0.001	p < 0.001
Day 90	-2.1 (-15.9%)	p < 0.001	-6.0 (-46.3%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by t-test , $p < 0.05$ is significant

Table 2. % Responders (greater than 20% decrease in hair loss)

	Placebo		Cynatine® HNS	
	Responders >20%	Responders <20%	Responders >20%	Responders <20%
Day 30	11/50 (22.0%)	39/50 (78.0%)	32/50 (64.0%)	18/50 (36.0%)
Day 60	5/50 (10.0%)	45/50 (90.0%)	48/50 (96.0%)	2/50 (4.0%)
Day 90	17/50 (34.0%)	33/50 (66.0%)	50/50 (100%)	0/50 (0%)

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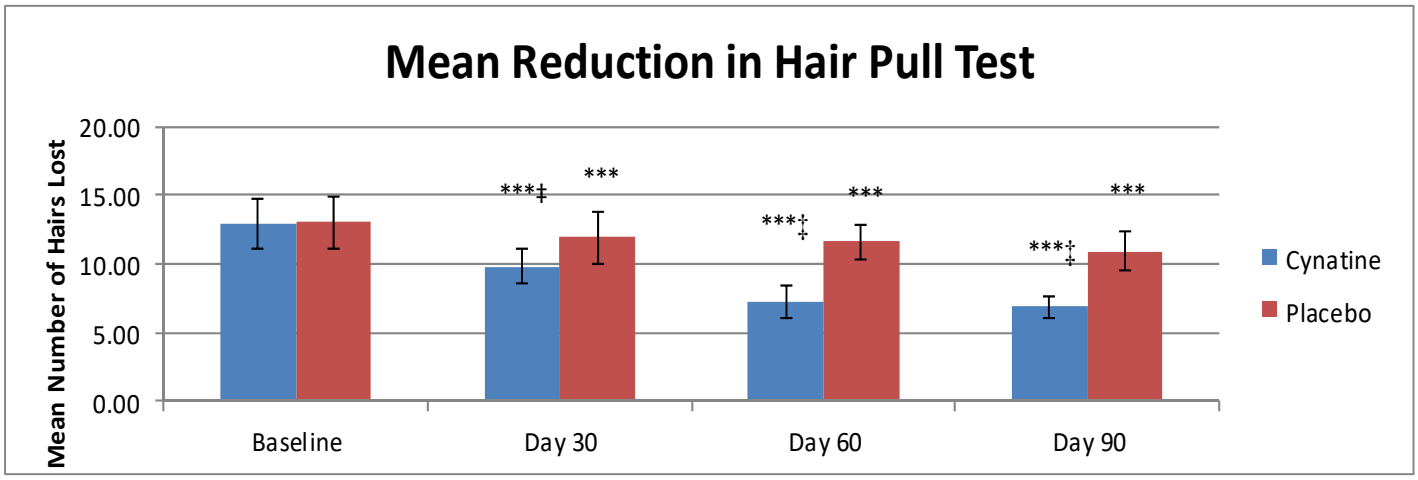

Figure 1. Hair Pull Test scores for Cynatine and Placebo.
* p <0.05, ** p<0.01, p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

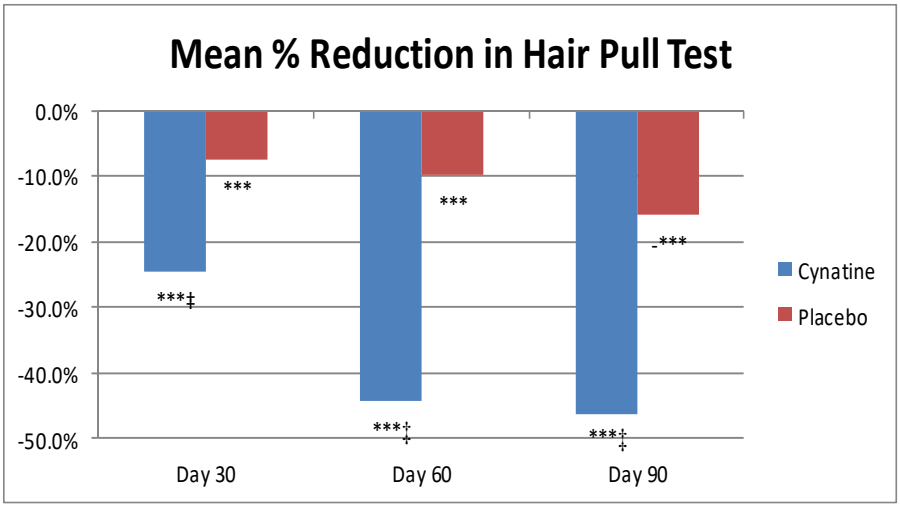

Figure 2. Hair Pull Test Mean % reduction from baseline for Cynatine and Placebo.
* p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine reduced hair loss over 3 times over Placebo at 30 (3.2x) and 4 Times at 60 days (4.5)
- Cynatine showed a statistically significant change to both baseline and Placebo at 30 days
- Cynatine was statistically significant to baseline and placebo at all time points
- 100% of the Cynatine group had a minimum decrease in hair loss of at least 20%, compared to placebo where only 34.0% showed a reduction of 20% or more
- 95% of the Cynatine group showed had a decrease of 30% and 72% had a decrease of 40% at 90 days.

Possible Structure Function Claims:

- Reduced hair loss from everyday activities
- Reduced hair loss from everyday activities can be seen within 30 days
- Supports Healthy Hair Growth

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b. Anagen/Telogen Phase Hair Test

- In order to measure the number of hairs in the Anagen and Telogen phase of the hair cycle, a 1.8cm^2 patch of hair was shaved and dyed for contrast.
- Photos were taken immediately after shaving and then again after 2 days using a close-up digital camera (TrichoScan®)
- Computer software then analyzes the two photographs and can determine how many hairs are growing (Anagen phase) and how many hairs are dead (Telogen phase)

Table 3. Analyses (Hair– Anagen/Telogen Phase)

Anagen/Telogen Score	Study Group				
	Placebo		Cynatine® HNS		
	Anagen Mean ± SD %	Telogen Mean % ± SD	Anagen Mean ± SD	Telogen Mean ± SD	p-value between groups
Baseline	149.9 ± 15.4	55.8 ± 9.0	148.1 ± 25.4	56.1 ± 10.4	
Day 90	157.2 ± 14.0	51.4 ± 6.2	179.9 ± 25.0	34.2 ± 12.2	
Change to Baseline:					
Day 90	7.3	-4.4	31.8	-21.9	p < 0.001
(Min,Max)	(-5.7, 15.9)	(16.2, -30.2)	(7.4, 46.7)	(-13.5, -70.2)	
P value(vs. baseline)	p < 0.001	p < 0.001	p <0.001	p < 0.001	

Intragroup p values determined by t-test, Intergroup values determined by t-test , p< 0.05 is significant

Table 4. % Responders

	Placebo		Cynatine® HNS	
	Responders >10%	Responders <10%	Responders >10%	Responders <10%
Day 90—AN	8/50 (16%)	42/50 (84%)	47/50 (94%)	3/50 (6%)
TEL	21/50 (42%)	29/50 (58%)	50/50 (100%)	0/50 (0%)

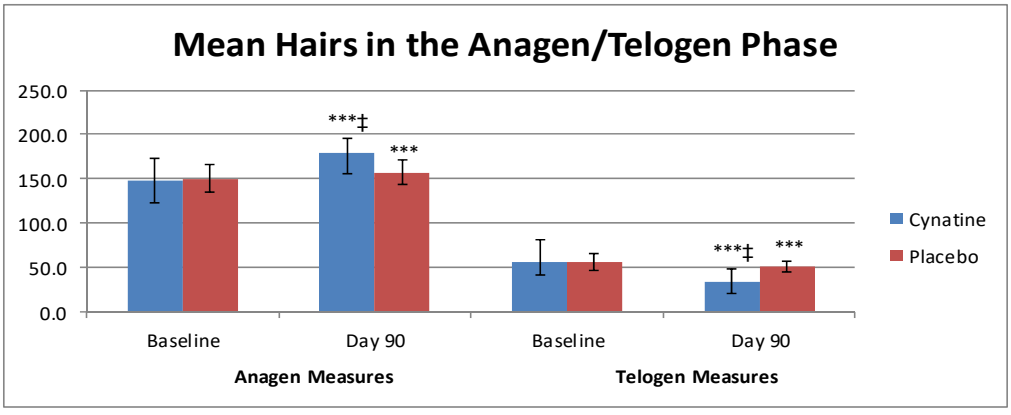

Figure 3. % of hairs in the Anagen and Telogen phase for Cynatine and Placebo.
*p <0.05, ** p<0.01, ***p<0.001 within group to baseline,
‡ p <0.001 between groups to baseline

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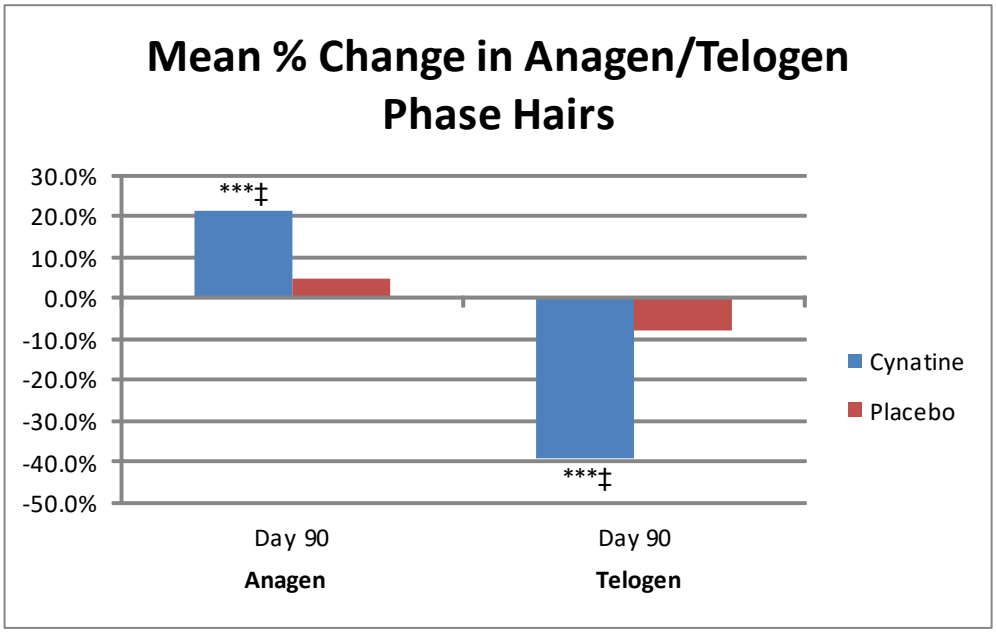

Figure 4. Mean % change in hairs in the Anagen and Telogen Phase for Cynatine and Placebo.
* p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine increases the number of hairs in the Anagen phase after 90 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 90 days
- Over 90% of subjects on Cynatine had at least a 10% increase in hairs in the Anagen phase, whereas less than 20% had the same effect on placebo
- Cynatine's effect over placebo was greater than 4-5 times more

Structure Function Claims:

- Cynatine supports healthy hair growth

c. Amino Acid Analysis of Hair

- Hair samples are taken from individuals and their amino acid profiles are analyzed by reverse phase liquid chromatography (results reported as % of total protein content)
- The main amino acids which deal with the health of hair are Serine, Glutamic Acid, Cystine and Methionine which is why these are measured.

Table 5. Analyses (Hair– Amino Acid)

Amino Acid Score	Study Group				
	Cynatine® HNS				
	Serine Mean % ± SD %	Glutamic Acid Mean % ± SD %	Cystine Mean % ± SD %	Methionine Mean % ± SD %	p value between groups
Baseline	11.0 ± 2.5	14.3 ± 2.6	17.4 ± 2.8	1.1 ± 0.6	
Day 90	15.4 ± 3.7	18.1 ± 2.9	26.8 ± 3.9	4.7 ± 1.5	
Difference	4.4	3.8	9.4	3.6	
Change to Baseline:					
Day 90 (% increase)	41.1%	26.8%	51.4%	332.3%	For all values
(Min,Max)	(-12.7, 84.1)	(-12.3, 76.6)	(-6.6, 169.7)	(-21.7, 1933.3)	p < 0.001
p value (vs. baseline)	p < 0.001	p < 0.001	p < 0.001	p < 0.001	

Intragroup p values determined by t-test, Intergroup values determined by t-test , p< 0.05 is significant

Table 6. Analyses (Hair– Amino Acid)

Amino Acid Score	Study Group				
	Placebo				
	Serine Mean % ± SD %	Glutamic Acid Mean % ± SD %	Cystine Mean % ± SD %	Methionine Mean % ± SD %	p value between groups
Baseline	11.3 ± 2.6	13.9 ± 3.4	17.8 ± 3.4	1.16 ± 0.6	
Day 90	11.7 ± 2.4	14.1 ± 3.7	16.9 ± 3.0	1.21 ± 0.6	
Difference	0.4	0.2	-1.1	0.05	
Change to Baseline:					
Day 90 (% increase)	3.2%	1.2%	-4.7%	4.3%	
(Min,Max)	(-24.1, 63.9)	(-27.6, 43.6)	(-31.1, 26.4)	(-61.1, 200)	
p value (vs. baseline)	n.s.	n.s.	p < 0.05	n.s.	

Intragroup p values determined by t-test, p< 0.05 is significant

Table 7. % Responders at Day 90

	Placebo		Cynatine® HNS	
	Responders >5%	Responders <5%	Responders >5%	Responders <5%
Serine	24/50 (48%)	26/50 (52%)	42/50 (84%)	8/50 (16%)
Glutamic Acid	20/50 (40%)	30/50 (60%)	41/50 (82%)	9/50 (18%)
Cystine	14/50 (28%)	36/50 (72%)	46/50 (92%)	4/50 (8%)
Methionine	28/50 (56%)	22/50 (44%)	48/50 (96%)	2/50 (4%)

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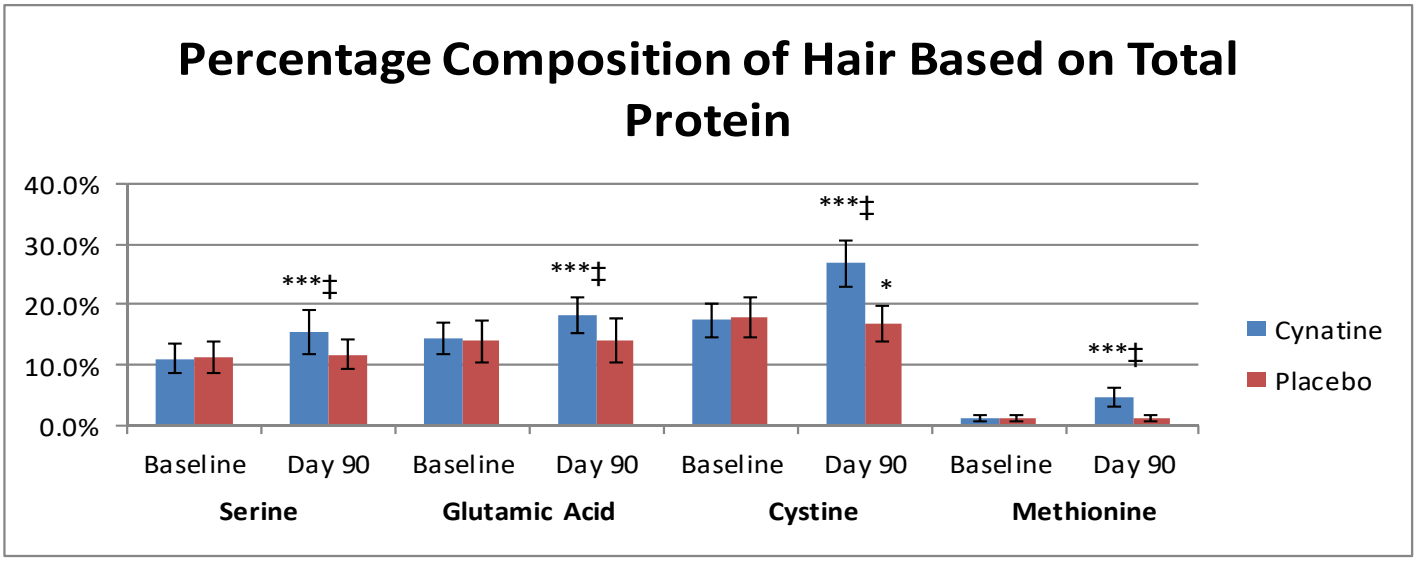

Figure 5. % of total protein composition of hair for Cynatine and Placebo.
* p <0.05, ** p<0.004, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

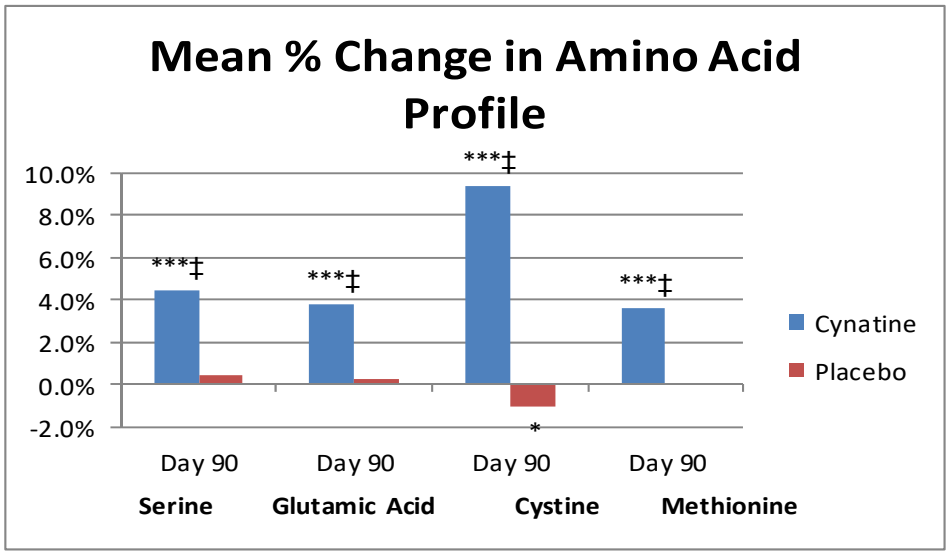

Figure 6. Mean % change in Amino Acid profile for Cynatine and Placebo.
* p <0.05, ** p<0.004, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine increases the amino acid content of Serine, Glutamic Acid, Cystine and Methionine after 90 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 90 days
- Over 80% of subjects on Cynatine had at least a 5% increase in Serine and Glutamic Acid, where as less than 50% had the same effect on placebo
- Over 90% of subjects had at least a 5% increase in Cystine and Methionine, where as less than 30% had a similar response for Cystine on placebo and less than 60% for Methionine

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- Cynatine's effect over placebo was a minimum of 8.5x times greater and a maximum of 72x times greater
- The ability of the hair to absorb the amino acids from Cynatine shows its bioavailability

Structure Function Claims:

- Cynatine supports healthy hair growth
- Cynatine improves the structure of hair
- Cynatine is bioavailable

d. Resistance to Traction

- The strength of the hair is measured by dynamometer and recorded in centiNewtons
- The stronger the hair is, the more force it will take to break

Table 8. Analyses (Hair– Resistance to Traction)

Resistance to Traction	Study Group		
	Placebo	Cynatine® HNS	
	Mean ± SD	Mean ± SD	p-value between groups
Baseline	71.2 ± 7.97	71.7 ± 7.47	
Day 90	71.6 ± 7.88	78.1 ± 7.79	
Change to Baseline:			
Day 90	0.4	6.4	p < 0.001
(Min,Max)	(-9.6, 9.4)	(-2.5, 21.2)	
P value (vs. baseline)	n.s.	p < 0.001	

Intragroup p values determined by t-test, Intergroup values determined by t-test , p< 0.05 is significant

Table 9. % Responders

	Placebo		Cynatine® HNS	
	Responders >2%	Responders <2%	Responders >2%	Responders <2%
Day 90	24/50 (48%)	26/50 (52%)	44/50 (88%)	6/50 (12%)

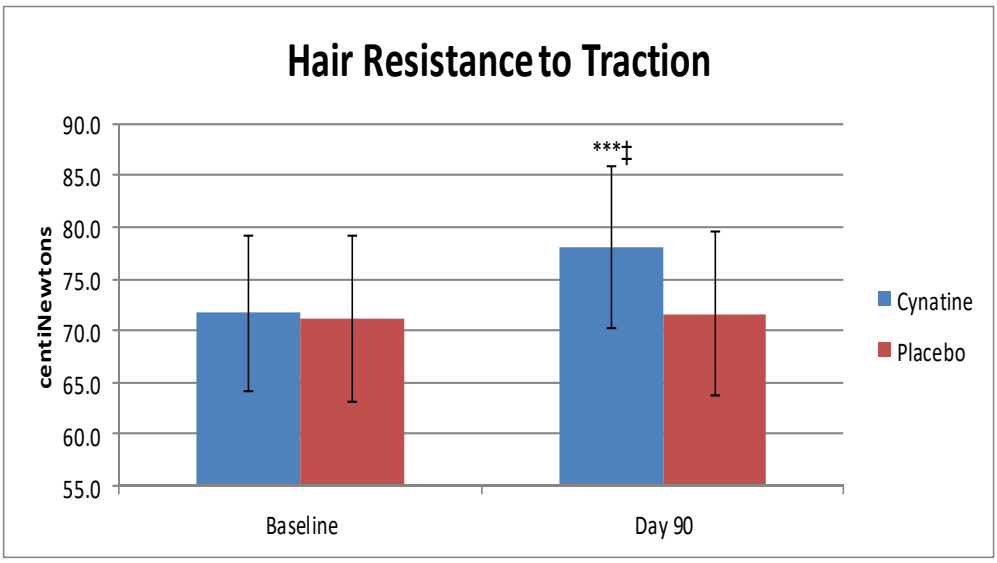

Figure 7. Hair resistance to traction results for Cynatine and Placebo. * p <0.05, ** p<0.004, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

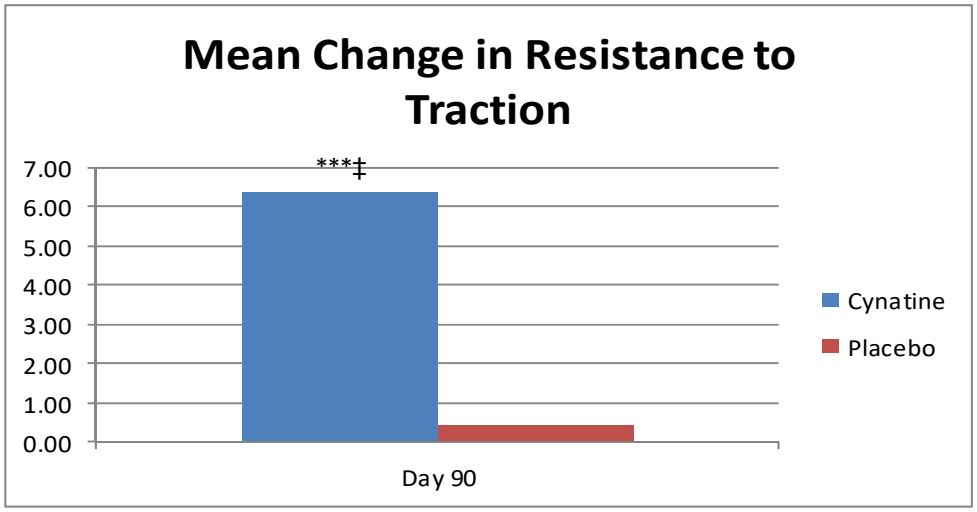

Figure 8. Mean change in resistance to traction for Cynatine and Placebo. * p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine increases the strength of hair after 90 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 90 days
- 88% of subjects on Cynatine had at least a 2% increase in the force need to break the hair, whereas less than 50% had the same effect on placebo
- Cynatine's effect over placebo was 16x greater than the mean increases on Placebo

Structure Function Claims:

- Cynatine supports healthy hair
- Cynatine improves the structure of hair
- Cynatine improves the strength of hair

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e. Hair Brightness Analysis

- Hair Brightness is measured by clinical evaluation by a trained clinician
- The condition of the hair is given a numerical value based on the following scale:

  1 (Hair is dull and devoid of brightness)

  2 (Hair is basically dull and not so bright)

  3 (Hair is shiny and bright)
- Changes in the condition of hair are evaluated at each time period and a new number on the scale is assigned to the subject if there is any change

Table 10. Analyses (Hair– Brightness Test)

Hair Brightness	Study Group				
	Placebo		Cynatine® HNS		
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	p-value between groups
Baseline	1.60 ± 0.5		1.60 ± 0.5		
Day 30	1.70 ± 0.5		1.90 ± 0.6		
Day 60	1.80 ± 0.5		2.50 ± 0.5		
Day 90	1.90 ± 0.5		2.60 ± 0.5		
Change to Baseline:					
Day 30	0.10 (6.2%)	p < 0.05	0.30 (18.5%)	p < 0.001	p < 0.05
Day 60	0.20 (13.6%)	p < 0.01	0.90 (55.6%)	p < 0.001	p < 0.001
Day 90	0.30 (19.8%)	p < 0.001	1.00 (59.3%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by t-test, p< 0.05 is significant

Table 11. % Responders

	Placebo		Cynatine® HNS	
	Responders >2 units	Responders > 1 unit	Responders >2 units	Responders > 1 Unit
Day 30	0/18 (0%)	4/50 (8%)	0/19 (0%)	17/50 (34%)
Day 60	0/18 (0%)	10/50 (20%)	1/19 (5.2%)	44/50 (88%)
Day 90	0/18 (0%)	14/50 (28%)	2/19 (10.5%)	46/50 (92%)

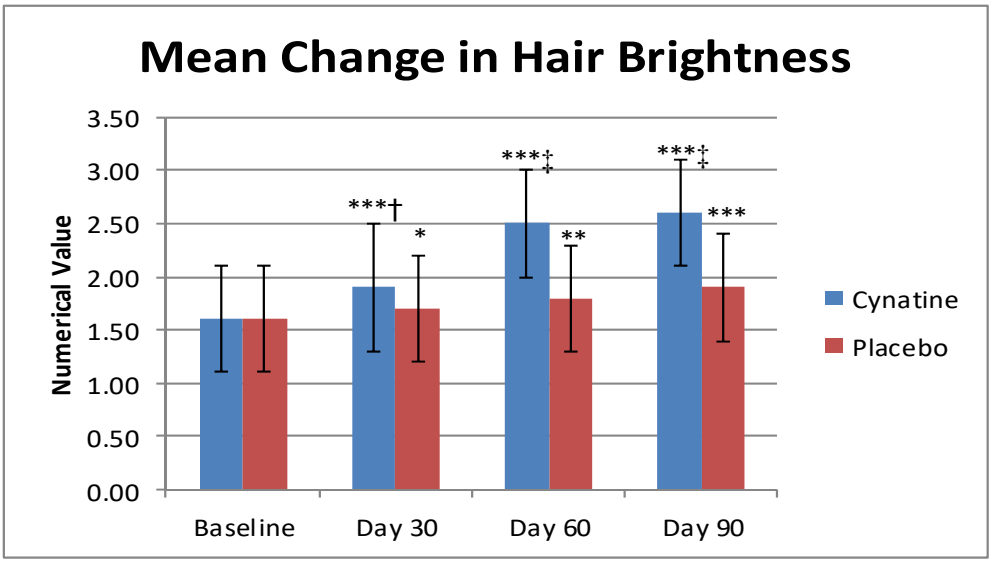
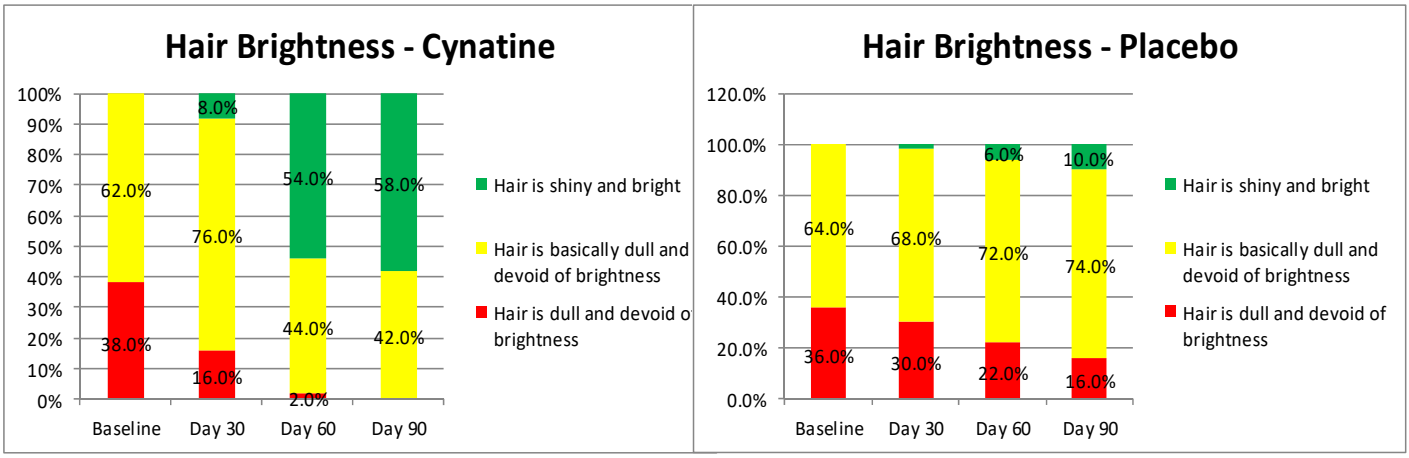


Figure 9. Hair brightness results for Cynatine and Placebo.
* p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.05, ‡ p <0.001 between groups to baseline



Figures 10 & 11. Percentage of subjects with each of the three determinations for hair brightness in the Cynatine and Placebo groups

Conclusion:

- Cynatine increases the shine and brightness of hair after 30 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 30,60, and 90 days
- Over 90% of subjects on Cynatine had at least a 1 unit increase in the look of their hair, where as less than 30% had the same effect on placebo
- Of the subjects which started with a hair score of 1 (allowing for 2 units of improvement) over 10% improved by 2 units on Cynatine, while 0 subjects improved by 2 units on placebo

Structure Function Claims:

- Cynatine supports healthy hair
- Cynatine improves the shine and brightness of hair

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2. Evaluation of Cynatine on Skin

This section looks at 7 different test evaluating Cynatine's effect on Skin

a. Skin Moisture

- The measurement of skin moisture is performed using the Internationally recognized CORNOMETER® method which measures the dielectric constant of water.
- This measurement is better than the impedance measurement because no galvanic relation between the device and the measuring object or polarization exists.

Table 12. Analyses (Skin– Moisturization)

Moisturization	Study Group				
	Placebo		Cynatine® HNS		
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	p-value between groups
Baseline	39.5 ± 7.0		40.4 ± 7.7		
Day 30	38.7 ± 6.6		42.8 ± 7.8		
Day 60	38.4 ± 6.3		44.4 ± 7.9		
Day 90	38.6 ± 6.1		45.1 ± 7.9		
Change to Baseline:					
Day 30	-0.8 (-4.2%)	p <0.05	2.5 (6.1%)	p < 0.001	p < 0.01
Day 60	-1.0 (-4.8%)	p < 0.01	4.0 (9.9%)	p < 0.001	p < 0.001
Day 90	-0.9 (-4.4%)	p < 0.05	4.7 (11.7%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by t-test , p< 0.05 is significant

Table 13. % Responders

	Placebo		Cynatine® HNS	
	Responders >0%	Responders <0%	Responders > 0%	Responders < 0%
Day 30	19/50 (38.0%)	31/50 (62.0%)	45/50 (90.0%)	5/50 (10.0%)
Day 60	13/50 (26.0%)	37/50 (74.0%)	49/50 (98.0%)	1/50 (2.0%)
Day 90	21/50 (42.0%)	29/50 (58.0%)	48/50 (96.0%)	2/50 (4.0%)

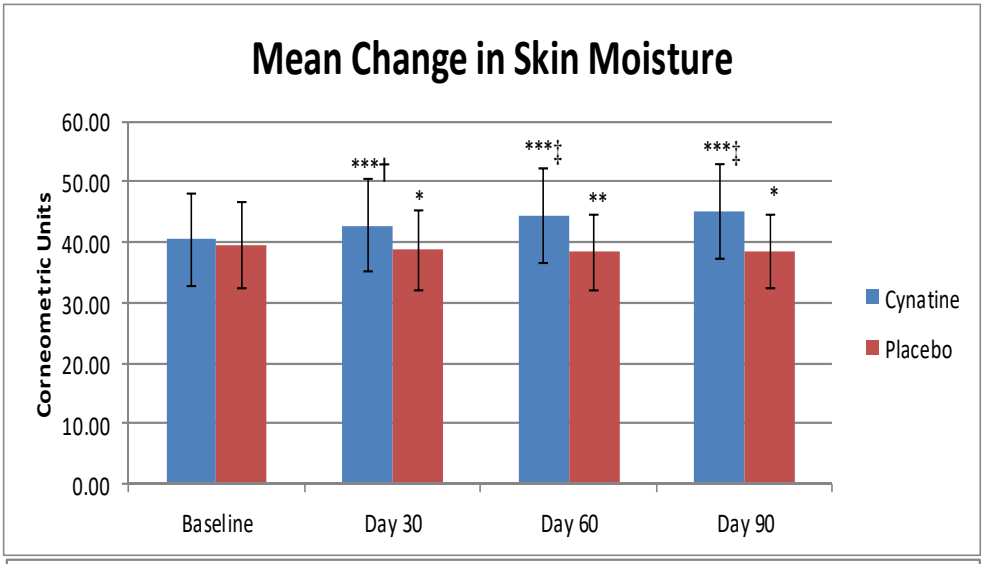

Figure 12. Mean change in skin moisture for Cynatine and Placebo.
*p <0.05, ** p<0.01, ***p<0.001 within group to baseline,
† p < 0.01, ‡ p <0.001 between groups to baseline

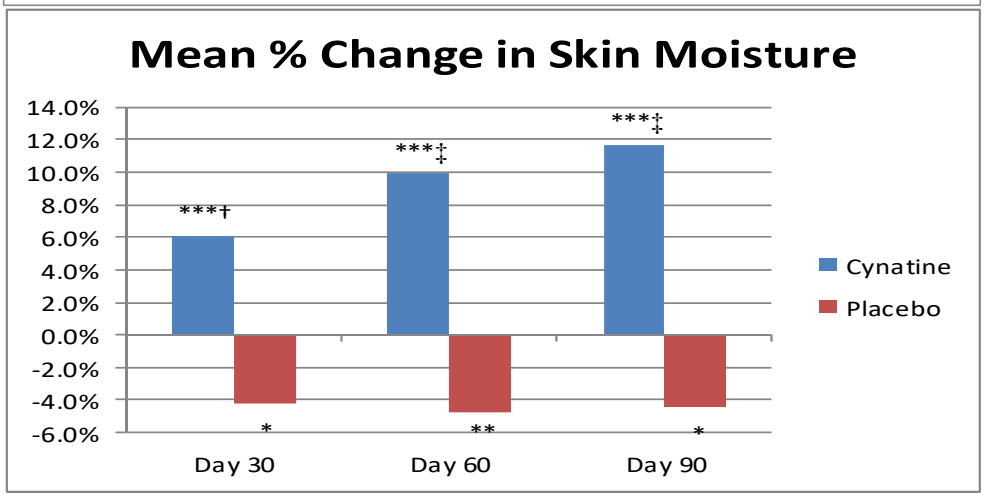

Figure 13. Mean % change in skin moisture for Cynatine and Placebo.
*p <0.05, ** p<0.01, ***p<0.001 within group to baseline,
† p < 0.01, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine increases the moisture of skin after 30 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 30, 60 and 90 days
- 90% of subjects on Cynatine had at least an increase in skin moisture at 30 days, whereas less than 40% had the same effect on placebo
- Cynatine increased skin moisture over placebo by over 5 times

Structure Function Claims:

- Cynatine supports healthy skin
- Cynatine improves the moisture of skin
- Cynatine helps to maintain skin moisture

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b. Skin Elasticity

- Skin elasticity is measured using the suction/elongation method and the successive release of skin inside the measurement probe, the CUTOMETER MPA 580.
- A constant negative pressure is applied to the skin followed by a return to normal conditions. An optical detection system is able to measure the results of both stages of this test and is able to provide an analysis of the skin to return to its normal state after deformation stress.

Table 14. Analyses (Skin– Elasticity)

Elasticity	Study Group				
	Placebo		Cynatine® HNS		
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	p-value between groups
Baseline	0.7191 ± 0.0870		0.7110 ± 0.0613		
Day 30	0.7207 ± 0.0801		0.7415 ± 0.0618		
Day 60	0.7192 ± 0.0869		0.7564 ± 0.0613		
Day 90	0.7375 ± 0.0893		0.7831 ± 0.0615		
Change to Baseline:					
Day 30	0.0016 (0.2%)	n.s.	0.0305 (4.3%)	p < 0.001	p <0.001
Day 60	0.0001 (0.0%)	n.s.	0.0454 (6.4%)	p < 0.001	p < 0.001
Day 90	0.0184 (2.6%)	p < 0.001	0.0721 (10.1%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by t-test , $p< 0.05$ is significant

Table 15. % Responders

	Placebo		Cynatine® HNS	
	Responders >2%	Responders <2%	Responders > 2%	Responders < 2%
Day 30	13/50 (26%)	37/50 (74%)	41/50 (82%)	9/50 (18%)
Day 60	15/50 (30%)	35/50 (70%)	43/50 (86%)	7/50 (14%)
Day 90	28/50 (56%)	22/50 (44%)	49/50 (98%)	1/50 (2%)

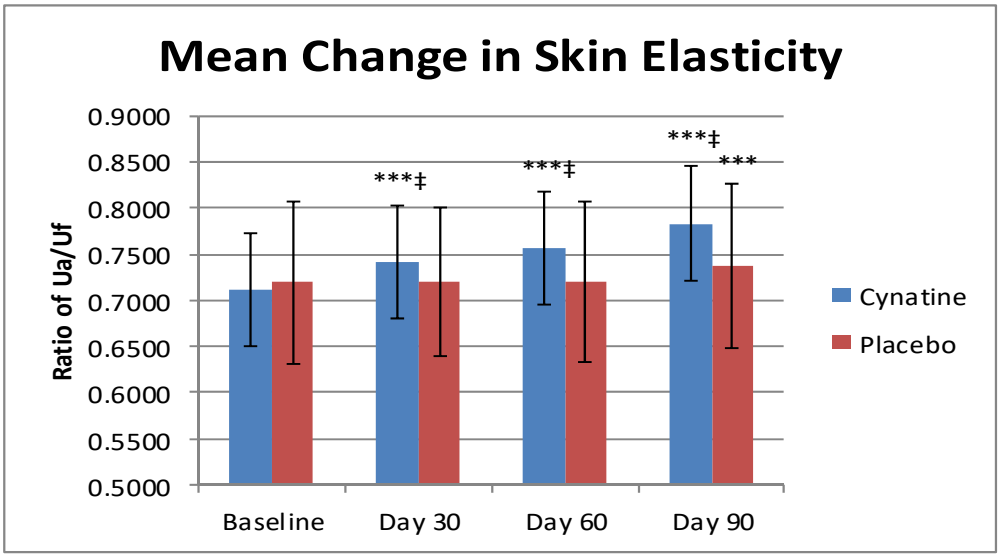

Figure 14. Mean Change in Skin Elasticity for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.01, ‡ p <0.001 between groups to baseline

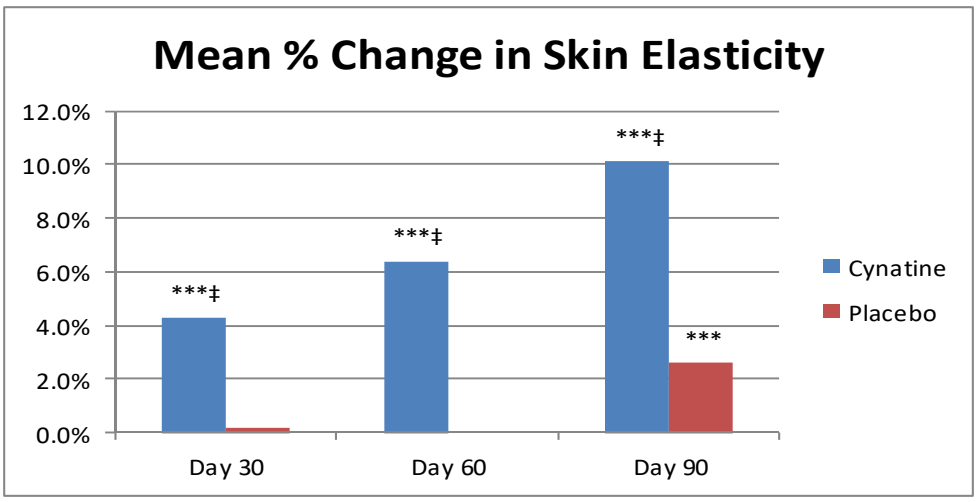

Figure 15. Mean % Change in Skin Elasticity for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.01, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine increases the elasticity of skin after 30 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 30, 60 and 90 days
- 80% of subjects on Cynatine had at least a2% increase in skin elasticity at 30 days, where as 26% had the same effect on placebo, this trend continued over the 60 and 90 day time periods
- Cynatine increased skin elasticity over placebo by almost 4x at 90 days

Structure Function Claims:

- Cynatine supports healthy skin
- Cynatine improves the elasticity of skin
- Cynatine helps to maintain skin elasticity

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c. Skin Wrinkles

- Skin wrinkle properties are measured by Primos 3D which is a device based on structured light projection. In conjunction with the comprehensive 3D measurement and evaluation software, the sensor evaluates skin properties.
- This test evaluates 3 separate measures of skin wrinkles, the Sa parameter (skin smoothness), the Sz parameter (skin roughness) and the wrinkle depth.

Table 16. Analyses (Skin– Smoothness Sa Parameter)

Smoothness	**Study Group**				
	Placebo		**Cynatine® HNS**		
	Mean ± SD	**p-value (v. Baseline)**	**Mean ± SD**	**p-value (v. Baseline)**	**p-value between groups**
Baseline	37.6 ± 8.4		36.5 ± 8.1		
Day 30	37.4 ± 8.7		35.3 ± 8.1		
Day 60	37.0 ± 8.9		34.1 ± 8.4		
Day 90	38.4 ± 9.4		32.2 ± 8.6		
Change to Base-line:					
Day 30	-0.2 (-0.5%)	n.s.	-1.6 (-4.7%)	p < 0.001	n.s.
Day 60	-0.6 (-1.4%)	n.s.	-2.5 (-7.3%)	p < 0.001	p < 0.01
Day 90	0.9 (2.3%)	n.s.	-3.5 (-10.1%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by t-test , $p < 0.05$ is significant

Table 17. % Responders

	Placebo		Cynatine® HNS	
	Responders >0%	Responders <0%	Responders > 0%	Responders < 0%
Day 30	24/50 (48%)	26/50 (52%)	14/50 (28%)	36/50 (72%)
Day 60	25/50 (50%)	25/50 (50%)	10/50 (20%)	40/50 (80%)
Day 90	30/50 (60%)	20/50 (40%)	4/50 (8%)	46/50 (92%)

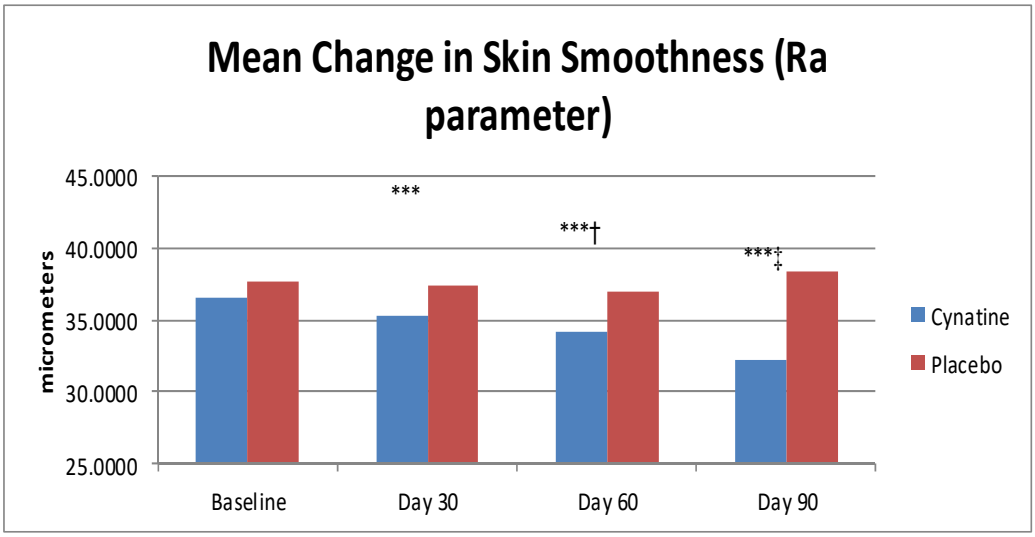

Figure 16. Mean change in skin smoothness for Cynatine and Placebo.
*p <0.05, ** p<0.01, ***p<0.001 within group to baseline,
† p <0.01, ‡ p <0.001 between groups to baseline

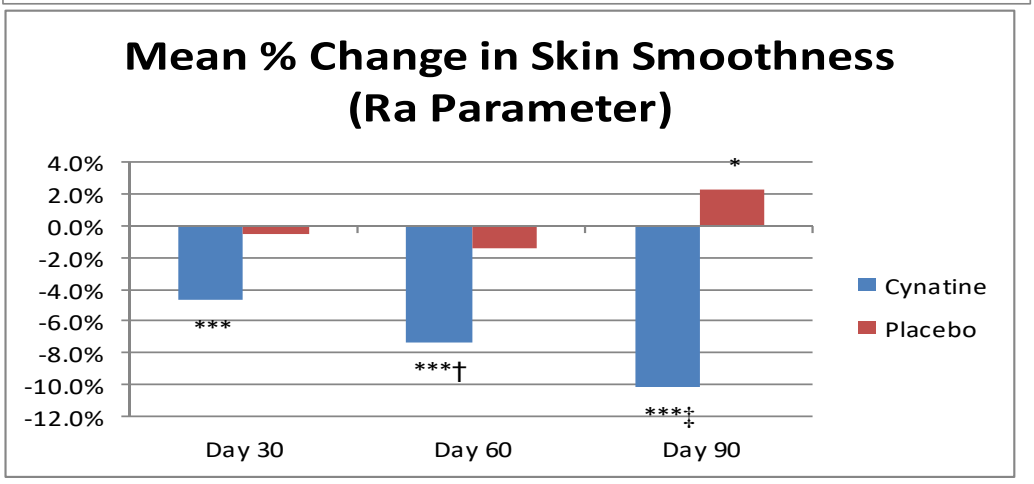

Figure 17. Mean % change in skin smoothness for Cynatine and Placebo.
*p <0.05, ** p<0.01, ***p<0.001 within group to baseline,
† p <0.01, ‡ p <0.001 between groups to baseline

Table 18. Analyses (Skin– Roughness Rz Parameter)

Roughness	Study Group				
	Placebo		Cynatine® HNS		
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	p-value between groups
Baseline	134.1 ± 28.4		137.0 ± 33.0		
Day 30	133.0 ± 30.3		133.1 ± 33.4		
Day 60	131.5 ± 29.4		129.9 ± 33.7		
Day 90	135.3 ± 33.2		124.8 ± 34.3		
Change to Baseline:					
Day 30	-1.1 (-0.8%)	n.s.	-3.9 (-2.6%)	p <0.01	n.s.
Day 60	-2.6 (-1.9%)	n.s.	-7.1 (-5.2%)	p < 0.001	p < 0.05
Day 90	1.2 (0.9%)	n.s.	-12.2 (-8.9%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by t-test , p< 0.05 is significant

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Table 19. % Responders (skin roughness)

	Placebo		Cynatine® HNS	
	Responders >0%	Responders <0%	Responders > 0%	Responders < 0%
Day 30	27/50 (54%)	23/50 (46%)	17/50 (34%)	33/50 (66%)
Day 60	23/50 (46%)	27/50 (54%)	14/50 (28%)	36/50 (72%)
Day 90	31/50 (62%)	19/50 (38%)	13/50 (26%)	37/50 (74%)

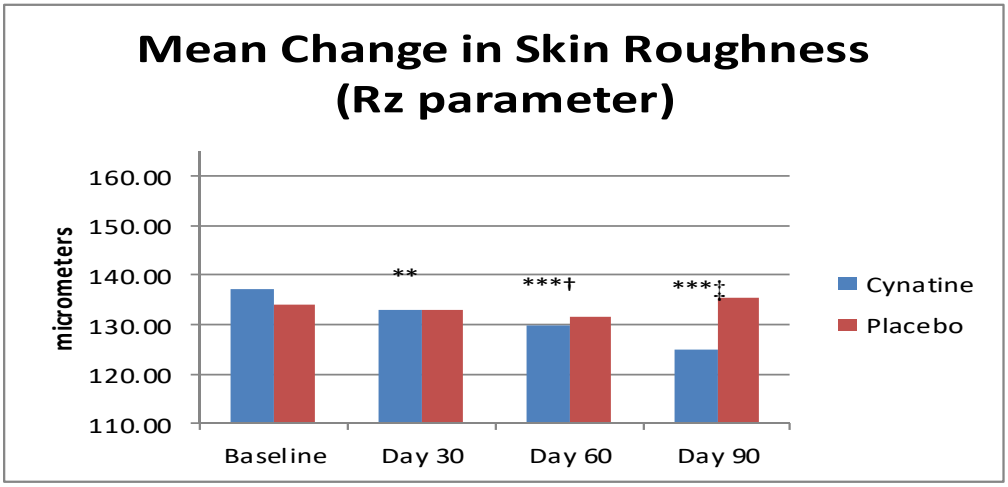

Figure 18. Mean Change in Skin roughness for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.05 ‡ p <0.001 between groups to baseline

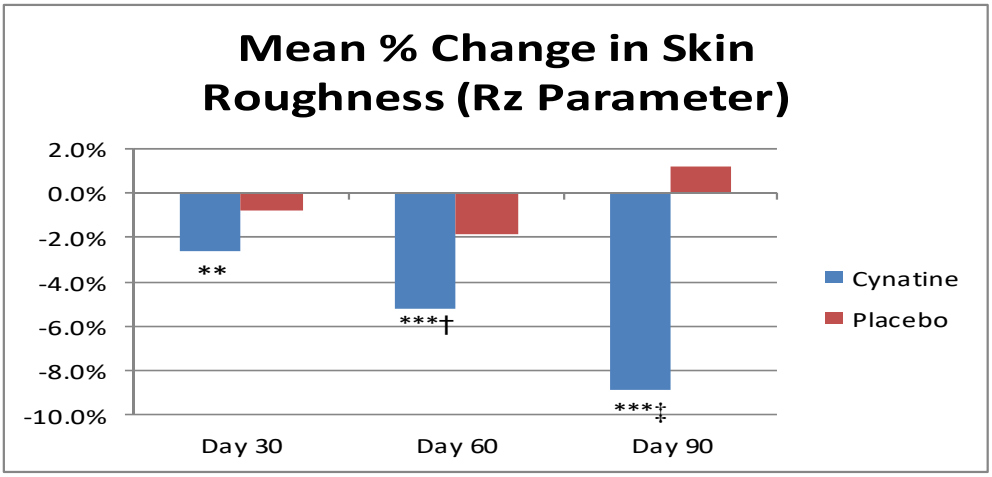

Figure 19. Mean Change in Skin roughness for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.05 ‡ p <0.001 between groups to baseline

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Table 20. Analyses (Skin– Wrinkle Depth)

Wrinkle Depth	Study Group				
	Placebo		Cynatine® HNS		
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	p-value between groups
Baseline	456.9 ± 117.7		454.7 ± 119.1		
Day 30	446.6 ± 116.3		432.8 ± 119.0		
Day 60	460.4 ± 115.4		401.9 ± 115.9		
Day 90	461.1 ± 118.4		391.6 ± 111.5		
Change to Baseline:					
Day 30	-10.2 (-2.2%)	p < 0.01	-22.0 (-4.8%)	p < 0.001	p < 0.05
Day 60	3.6 (0.8%)	n.s.	-52.8 (-11.6%)	p < 0.001	p < 0.001
Day 90	4.2 (0.9%)	n.s.	-63.1 (-13.9%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by t-test , p< 0.05 is significant

Table 21. % Responders

	Placebo		Cynatine® HNS	
	Responders >0%	Responders <0%	Responders > 0%	Responders < 0%
Day 30	22/50 (44%)	28/50 (56%)	16/50 (32%)	34/50 (68%)
Day 60	30/50 (60%)	20/50 (40%)	5/50 (10%)	45/50 (90%)
Day 90	30/50 (60%)	20/50 (40%)	0/50 (0%)	50/50 (100%)

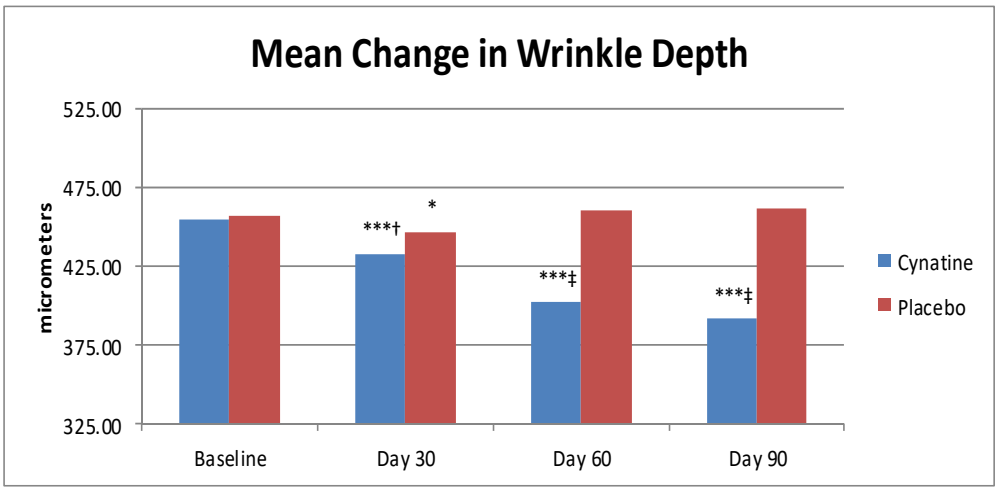

Figure 20. Mean change in wrinkle depth for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.05 ‡ p <0.001 between groups to baseline

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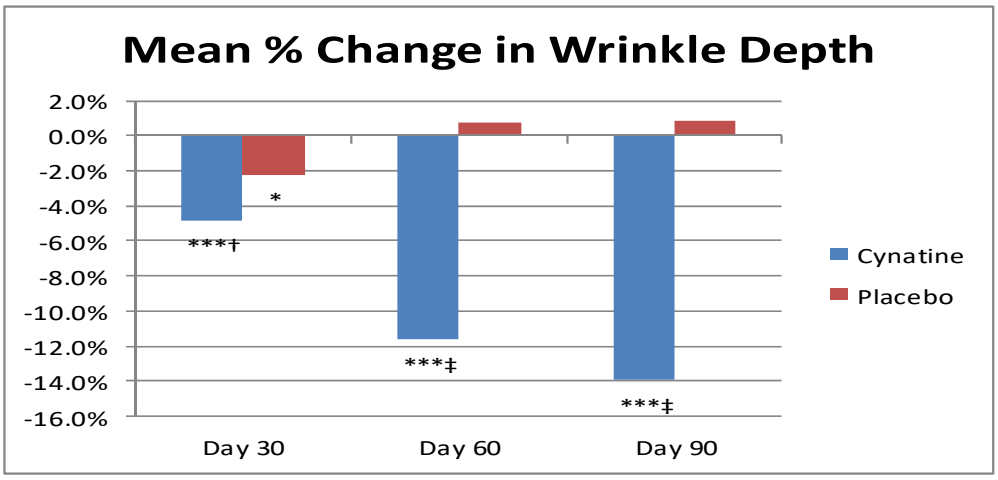

Figure 21. Mean % change in wrinkle depth for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.05 ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine significantly reduces skin wrinkles after 60 days according to all three measurements
- Cynatine showed results that were statistically significant to both baseline and placebo at 60 and 90 days in all three measurements
- Over 70% of subjects on Cynatine had a decrease in skin wrinkles at 60 days, where no more than 55% had the same effect on placebo
- Skin smoothness improved in 72% of subjects on Cynatine at 30 days and improves to over 90% by 90 Days, while placebo peaks at 52% at 30 days and decreases at each further time point
- Cynatine decreases skin wrinkles over placebo by approximately 9 to 14% depending on the measure

Structure Function Claims:

- Cynatine supports healthy skin
- Cynatine may reduce measures of skin wrinkles

d. Skin Cohesivity (Protein Content)

- The protein content of the skin is measured through samples of the stratum corneum being taken using CORNEOFIX Foil. The amount of protein remaining on the foil is measured and expressed in micrograms.

Table 22. Analyses (Skin– Cohesivity Protein Content)

Protein Content	Study Group		
	Placebo	Cynatine® HNS	
	Mean ± SD	Mean ± SD	p-value between groups
Baseline	37.3 ± 7.3	36.9 ± 8.0	
Day 90	37.6 ± 7.0	27.5 ± 7.8	
Change to Baseline:			
Day 90	0.3 (0.7%)	-9.4 (-25.5%)	p < 0.001
(Min,Max)	(17.8%, -21.7%)	(8.2%, -58.0%)	
P value (vs. baseline)	n.s.	p < 0.001	

Intragroup p values determined by t-test, Intergroup values determined by t-test , p< 0.05 is significant

Table 23. % Responders

	Placebo		Cynatine® HNS	
	Responders >0%	Responders <0%	Responders >0%	Responders <0%
Day 90	13/24 (54.2%)	11/24 (45.8%)	6/50 (12%)	44/50 (88%)

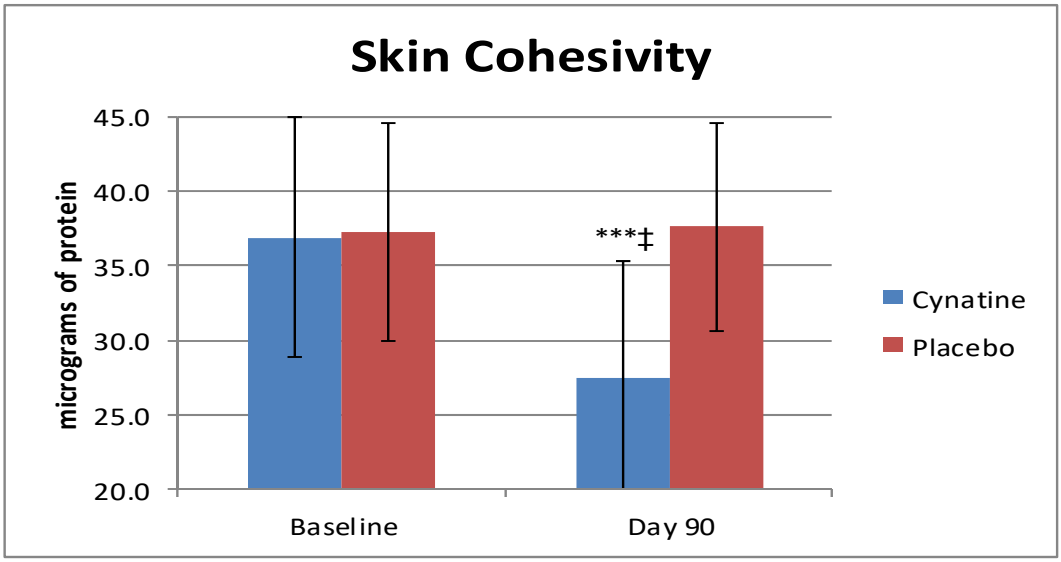

Figure 22. Mean % change in wrinkle depth for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

Note: Because skin cohesivity is measured by the amount of protein lost in the test, a negative measure is desired

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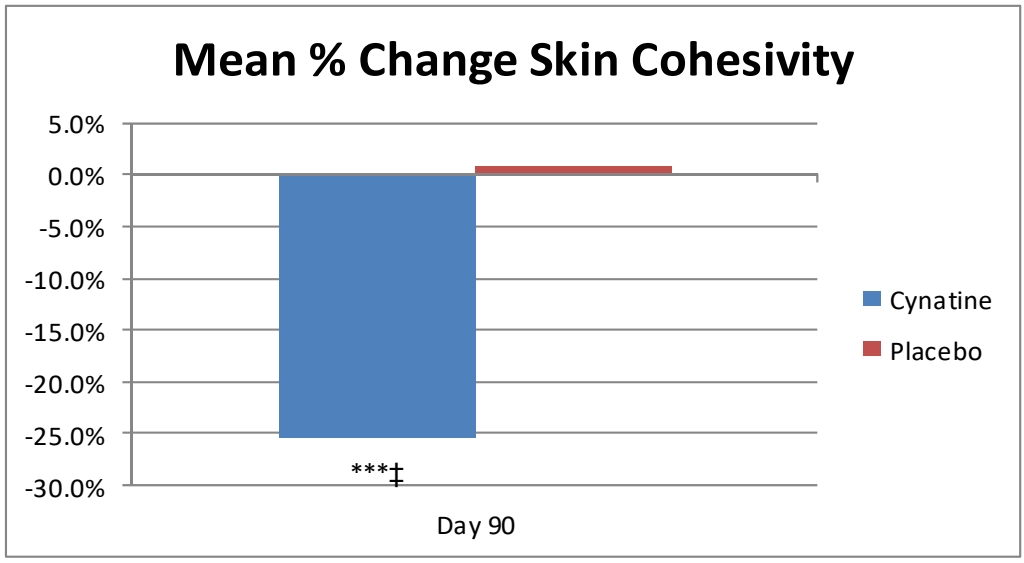

Note: Because skin cohesivity is measured by the amount of protein lost in the test, a negative measure is desired

Figure 23. Mean % change in wrinkle depth for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine improves the compactness and structure of skin after 90 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 90 days
- Over 85% of subjects on Cynatine had a decrease in the protein remaining on the test kit at 90 days, where as less than 46% had the same effect on placebo
- Cynatine is bioavailable based on its ability to improve the protein structure of skin namely the keratinocytes below the epidermis

Structure Function Claims:

- Cynatine supports healthy skin
- Cynatine improves the structure and cohesiveness of skin
- Cynatine is bioavailable

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3. Evaluation of Cynatine on Nails

This analysis focuses on multiple measures on nail health

a. Tendency to break

Nails are given a clinical evaluation by a trained professional based on the following standards:

1 (Nails are flaked or broken or have a tendency to break)

2 (Nails are moderately flaked or broken or have a tendency to break)

3 (Nails are neither flaked nor broken and don't have a tendency to break)

Improvements in the Nails over time are measured by the evaluator by the following standards:

1 (No variation)

2 (Slight improvement)

3 (Moderate Improvement)

4 (Remarkable Improvement)

Table 24. Analyses (Nails– Tendency to Break)

Tendency to break	**Study Group**		
	Placebo	**Cynatine® HNS**	
	Value ± SD	**Value ± SD**	**p-value between groups**
Baseline	1.5 ± 0.5	1.5 ± 0.5	
Change to Base-line: Day 30 Day 60 Day 90	 1.1 ± 0.3 1.1 ± 0.3 1.3 ± 0.4	 1.9 ± 0.7 2.1 ± 0.8 2.5 ± 0.8	 p < 0.001 p <0.001 p <0.001

Intergroup p values determined by t-Test, p <0.05 is significant

Table 25. % Responders

	Placebo		Cynatine® HNS	
	Responders > 1	Responders 1	Responders > 1	Responders 1
Day 90	13/50 (26%)	37/50 (74%)	47/50 (94%)	3/50 (6%)

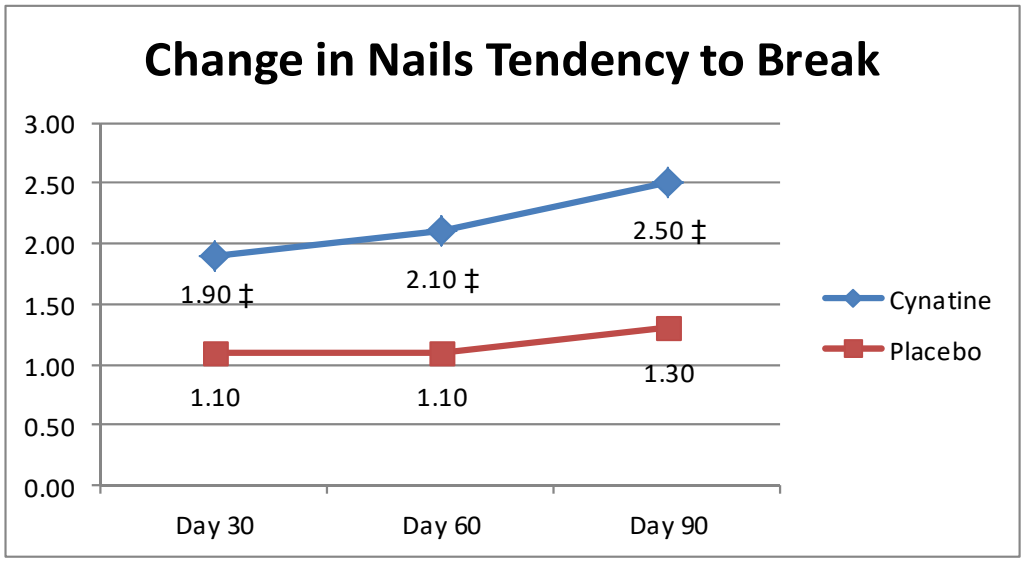

Figure 24. Change in Nails Tendency to Break for Cynatine and Placebo.
‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine decreases the nails tendency to break after 30 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 30, 60 and 90 days
- Over 90% of subjects on Cynatine had a decrease in the tendency of nails to break at 90 days, where as less than 30% had the same effect on placebo
- Cynatine decreases nails tendency to break by more than 2x placebo
- No placebo subject had a score of higher than 2, whereas 20 active subjects scored a 3 or 4

Structure Function Claims:

- Cynatine supports healthy nails
- Cynatine reduces nails tendency to break

b. Nail evaluation

- Nails are evaluated by a dermatologist based on the pairs in the chart below
- Each pair has two evaluation choices and add to 100%

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Table 26: Analyses (Nails various parameters)

	Parameter/Time	T0	T1	T2	T3	Δ T1	p value	Δ T2	p value	Δ T3	p value
Cynatine HNS	Hard	30%	70%	82%	90%	40%	<0.001	52%	<0.001	60%	<0.001
	Soft	70%	30%	18%	10%						
Placebo	Hard	28%	36%	38%	42%	8%		10%		14%	
	Soft	72%	64%	62%	58%						
Cynatine HNS	Resistant	28%	72%	82%	92%	44%	<0.001	54%	<0.001	64%	<0.001
	Fragile	72%	28%	18%	8%						
Placebo	Resistant	32%	42%	44%	52%	10%		12%		20%	
	Fragile	68%	58%	56%	48%						
Cynatine HNS	Broken	52%	28%	18%	10%						
	Not Broken	48%	72%	82%	90%	24%	<0.01	34%	<0.001	42%	<0.001
Placebo	Broken	48%	48%	40%	38%						
	Not Broken	52%	52%	60%	62%	0%		8%		10%	
Cynatine HNS	Rough	44%	30%	10%	2%						
	Smooth	56%	70%	90%	98%	14%	<0.05	34%	<0.001	42%	<0.001
Placebo	Rough	46%	44%	40%	38%						
	Smooth	54%	56%	60%	62%	2%		6%		12.5%	
Cynatine HNS	Yellowish	28%	20%	6%	4%						
	White (natural color)	72%	80%	94%	96%	8%	n.s.	22%	<0.05	24%	<0.05
Placebo	Yellowish	30%	28%	24%	24%						
	White (natural color)	70%	72%	76%	76%	2%		6%		6%	

Conclusion:

- Cynatine improves the health of nails
- Cynatine showed results that were statistically significant to both baseline and placebo at 30, 60 and 90 days, depending on the measure, with all significant after 60 days

Structure Function Claims:

- Cynatine supports healthy nails

Safety Results: The product was well tolerated during the study as 100% of the people surveyed gave it an excellent rating for tolerability. There were no dropouts in either the Active or Placebo groups of the study. There were no adverse events reported during the study. The two groups were homogenous for the relevant demographic data which could influence the study outcome.

This data confirms that Cynatine® HNS is safe to use under the suggested condition of use (500mg per day) for 90 days.

Study Demographics:

Active Dosage:	500mg Cynatine® HNS
Population:	100 men and women (50 active, 50 placebo, 25 men, 25 women each)
Randomization:	Randomized, double blinded placebo control study
Study time:	March 2019 through July 2019
Location:	Complife, Milan Italy

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