

Technical Summary of Cynatine[®] HNS Clinical Trial

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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 remain rooted, while hairs in the telogen phase should be extracted

Table 1. Analyses (Hair- Pull Test)

Pull Test Score	Study Group				
	Placebo		Cynatine [®] HNS		p-value between groups
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	
Baseline	9.00 ± 1.3		9.20 ± 1.3		
Day 30	8.60 ± 2.8		7.60 ± 1.4		
Day 60	8.60 ± 1.5		5.50 ± 1.0		
Day 90	7.90 ± 1.5		4.80 ± 0.9		
<u>Change to Baseline:</u>					
Day 30	-0.40 (4.4%)	n.s.	-1.60 (16.9%)	p < 0.001	n.s.
Day 60	-0.40 (4.4%)	n.s.	-3.70 (38.9%)	p < 0.001	p < 0.001
Day 90	-1.10 (12.2%)	p < 0.01	-4.40 (46.6%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by Mann Whitney U 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	12/25 (48.0%)	13/25 (52.0%)	11/25 (44.0%)	14/25 (56.0%)
Day 60	8/25 (32.0%)	17/25 (68.0%)	22/24 (91.6%)	2/24 (8.4%)
Day 90	9/24 (37.5%)	15/24 (62.5%)	24/24 (100%)	0/24 (0%)

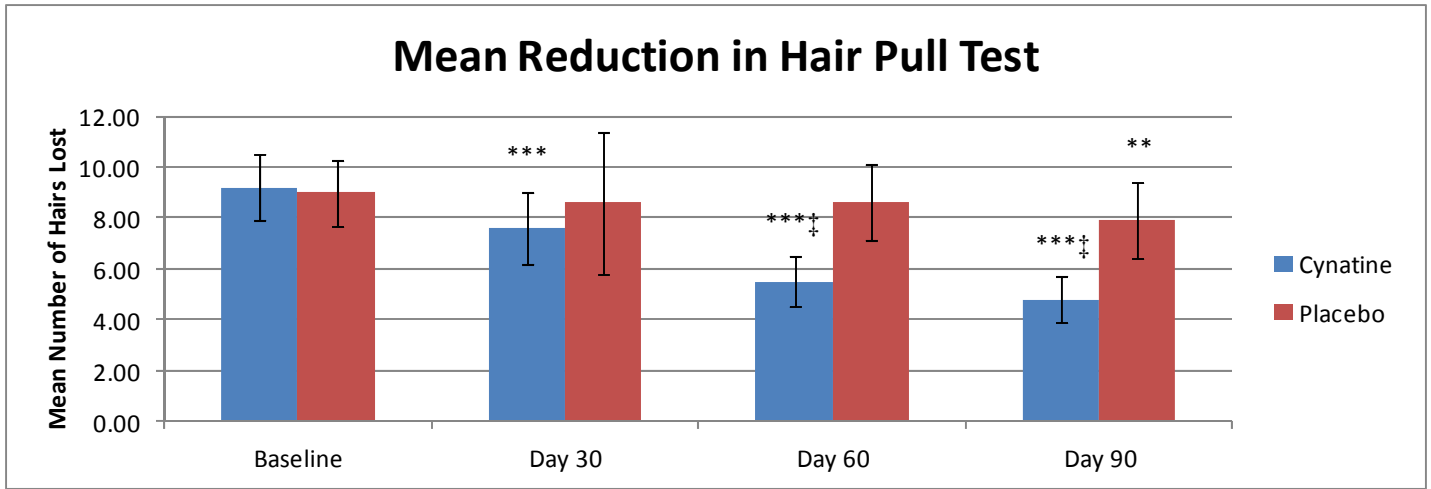


Figure 1. Hair Pull Test scores for Cynatine and Placebo.

* p <0.05, ** p<0.01, p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

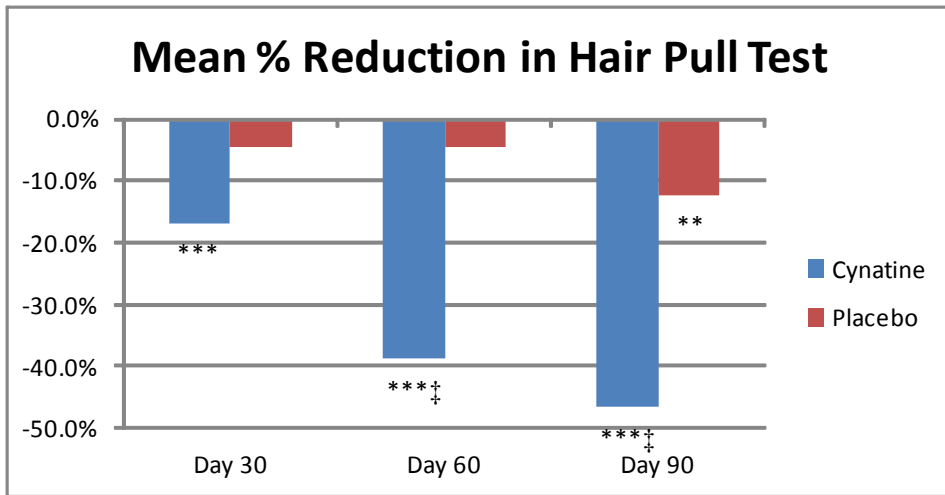


Figure 2. Hair Pull Test Mean % reduction from baseline for Cynatine and Placebo.

* 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 almost 4 times over Placebo at 30 days (3.8x)
- Cynatine showed a statistically significant change to both baseline and Placebo at 60 days
- Cynatine statistically significant to baseline at all time points and placebo at day 60 and 90
- Cynatine continued to show an almost 4 times increase in hair loss at 90 days (3.8x)
- 100% of the Cynatine group had a minimum decrease in hair loss of at least 20%, compared to placebo where only 37.5% showed a reduction of 20% or more

Possible Structure Function Claims:

- Reduced hair loss from everyday activities
- Reduced hair loss from everyday activities can be seen within 30 to 60 days
- Supports Healthy Hair Growth

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 1.8cm² 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
- 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				p-value between groups
	Placebo		Cynatine [®] HNS		
	Anagen Mean % ± SD %	Telogen Mean % ± SD %	Anagen Mean % ± SD %	Telogen Mean % ± SD %	
Baseline	71.7 ± 2.1	28.3 ± 2.1	70.6 ± 2.7	29.4 ± 2.7	
Day 90	72.8 ± 5.3	27.2 ± 5.3	79.80 ± 5.6	20.2 ± 5.6	
<u>Change to Baseline:</u>					
Day 90	1.1	-1.1	9.2	-9.2	p < 0.001
(Min,Max)	(-7.9, 9.5)	(-9.5, 7.9)	(2.1, 16.5)	(-16.5, -2.1)	
P value(vs. baseline)	n.s.	n.s.	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 >4%	Responders <4%	Responders >4%	Responders <4%
Day 90	7/24 (29.2%)	17/24 (70.8%)	22/24 (91.7%)	2/24 (8.3%)

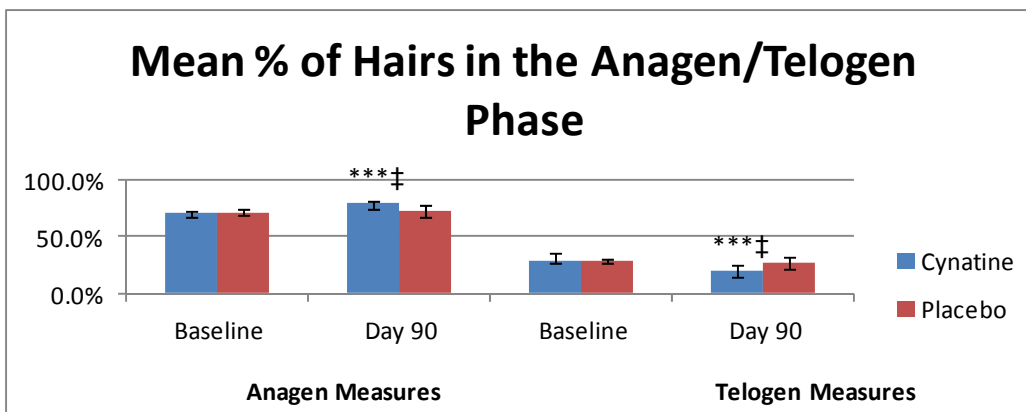


Figure 3. % of hairs in the Anagen and Telogen phase for Cynatine and Placebo.
 *p <0.05, ** p<0.01, ***p<0.001 within group to baseline,
 ‡ p <0.001 between groups to baseline

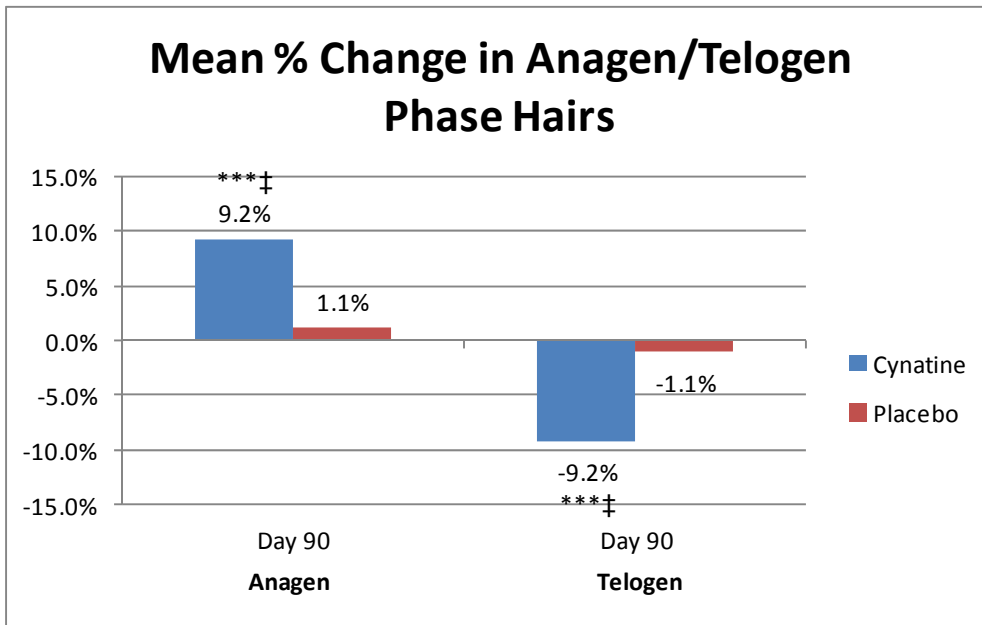


Figure 4. Mean % change in hairs in the Anagen and Telogen Phase for Cynatine and Placebo.

* 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 4% increase in hairs in the Anagen phase, whereas less than 30% had the same effect on placebo
- Cynatine's effect over placebo was greater than 8 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				p value between groups
	Serine Mean % ± SD %	Glutamic Acid Mean % ± SD %	Cystine Mean % ± SD %	Methionine Mean % ± SD %	
Baseline	10.5 ± 1.8	13.1 ± 2.3	16.0 ± 2.4	0.8 ± 0.3	
Day 90	13.6 ± 3.0	16.6 ± 3.5	24.6 ± 5.2	5.6 ± 3.0	
<u>Change to Baseline:</u>					
Day 90	3.2%	3.5%	8.6%	4.8%	For all values p < 0.001
(Min,Max)	(-0.5, 6.5)	(-1.6, 7.5)	(-0.6, 17.5)	(-0.1, 8.8)	
p value (vs. baseline)	p < 0.001	p < 0.001	p < 0.001	p < 0.004	

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				p value between groups
	Serine Mean % ± SD %	Glutamic Acid Mean % ± SD %	Cystine Mean % ± SD %	Methionine Mean % ± SD %	
Baseline	10.6 ± 1.8	13.7 ± 2.0	15.8 ± 1.8	0.7 ± 0.3	
Day 90	10.8 ± 1.7	13.4 ± 1.9	16.3 ± 2.5	1.2 ± 0.8	
<u>Change to Baseline:</u>					
Day 90	0.2%	-0.4%	0.6%	0.5%	
(Min,Max)	(-3.2, 3.2)	(-2.9, 3.2)	(-1.9, 3.5)	(-0.4, 2.1)	
p value (vs. baseline)	n.s.	n.s.	n.s.	p < 0.004	

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

Table 7. % Responders at Day 90

	Placebo		Cynatine® HNS	
	Responders >2%	Responders <2%	Responders >2%	Responders <2%
Serine	1/24 (4.2%)	23/24 (95.8%)	17/24 (70.8%)	7/24 (29.2%)
Glutamic Acid	1/24 (4.2%)	23/24 (95.8%)	17/24 (70.8%)	7/24 (29.2%)
Cystine	4/24 (16.7%)	20/24 (83.3%)	20/24 (83.3%)	4/24 (16.7%)
Methionine	1/24 (4.2%)	23/24 (95.8%)	20/24 (83.3%)	4/24 (16.7%)

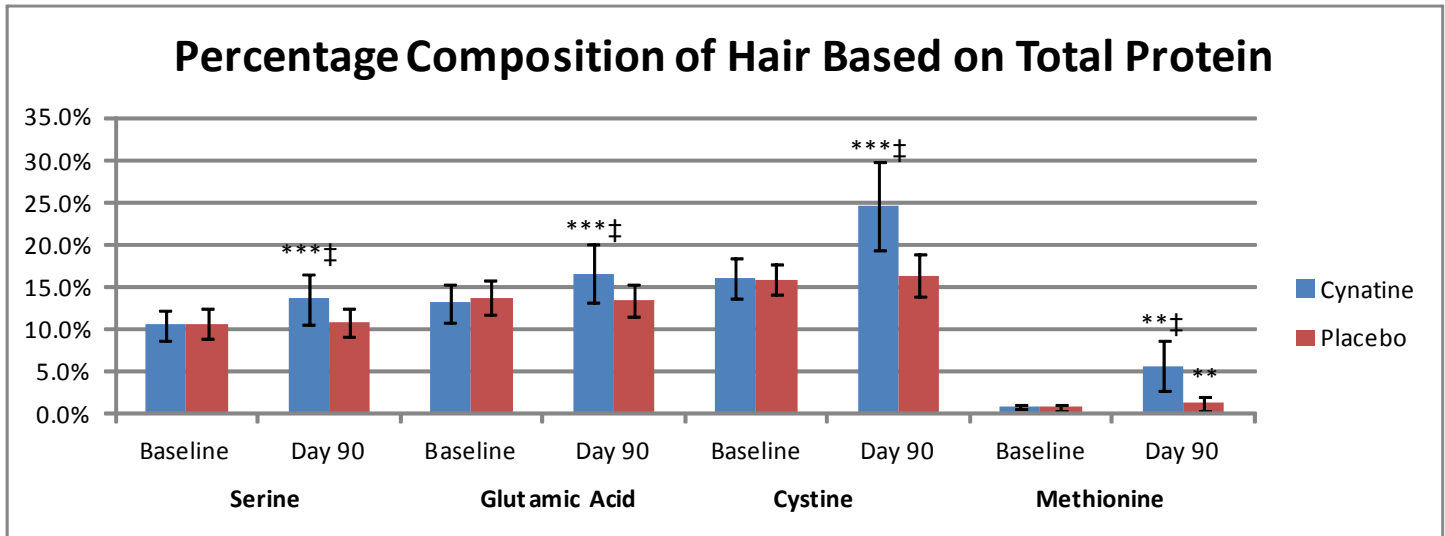


Figure 5. % of total protein composition of hair for Cynatine and Placebo.

* p <0.05, ** p<0.004, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

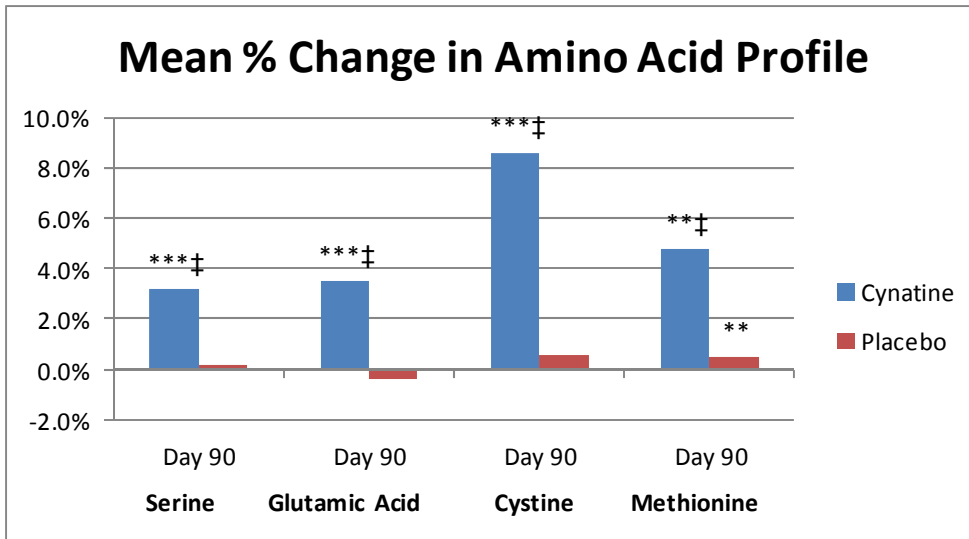


Figure 6. Mean % change in Amino Acid profile for Cynatine and Placebo.

* 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 70% of subjects on Cynatine had at least a 2% increase in Serine and Glutamic Acid, where as less than 5% had the same effect on placebo
- Over 80% of subjects had at least a 2% increase in Cystine and Methionine, where as less than 20% had a similar response for Cystine on placebo and less than 5% for Methionine

- Cynatine’s effect over placebo was greater as the max increases in placebo are less than the mean increases on Cynatine
- 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	69.9 ± 9.9	71.3 ± 9.3	
Day 90	69.6 ± 9.7	77.2 ± 8.3	
<u>Change to Baseline:</u>			
Day 90 (Min,Max)	-0.3 (-4.9, 3.9)	5.9 (-2.7, 18.7)	p < 0.001
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	3/24 (12.5%)	21/24 (87.5%)	18/24 (75%)	6/24 (25%)

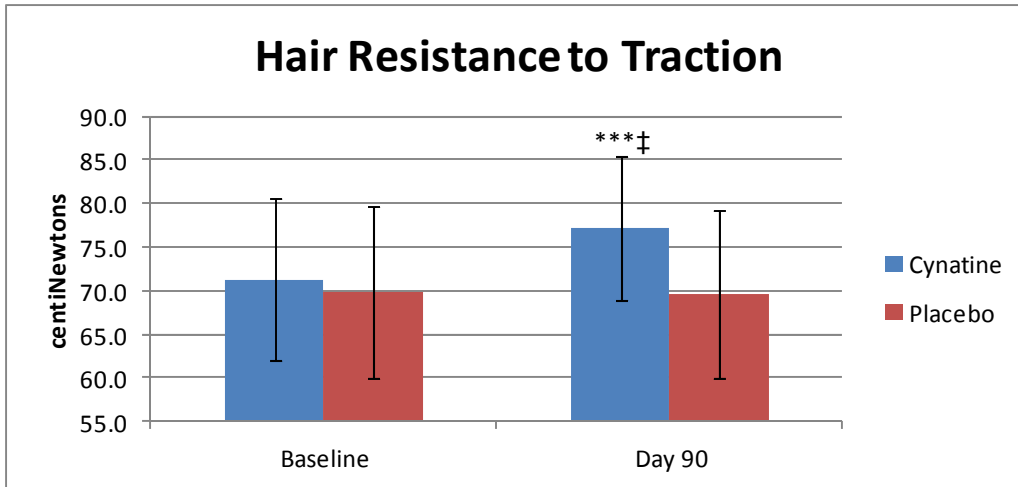


Figure 7. Hair resistance to traction results for Cynatine and Placebo. * p <0.05, ** p<0.004, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

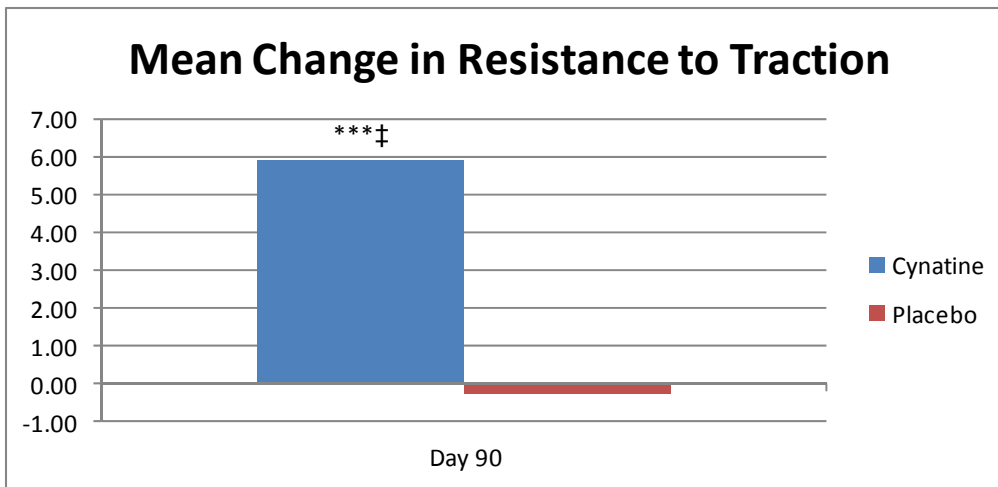


Figure 8. Mean % change in resistance to traction for Cynatine and Placebo. * p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

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
- 75% of subjects on Cynatine had at least a 2% increase in the force need to break the hair, whereas less than 15% had the same effect on placebo
- Cynatine’s effect over placebo was greater as the max increases in placebo are less than the mean increases on Cynatine

Structure Function Claims:

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

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)

Pull Test Score	Study Group				
	Placebo		Cynatine® HNS		p-value between groups
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	
Baseline	1.70 ± 0.5		1.70 ± 0.5		
Day 30	1.70 ± 0.5		2.00 ± 0.6		
Day 60	2.00 ± 0.6		2.60 ± 0.6		
Day 90	2.00 ± 0.6		2.80 ± 0.4		
<u>Change to Baseline:</u>					
Day 30	0.00 (0%)	n.s.	0.30 (17.6%)	p < 0.005	p < 0.02
Day 60	0.30 (17.6%)	p < 0.01	0.90 (52.9%)	p < 0.001	p < 0.001
Day 90	0.30 (17.6%)	p < 0.01	1.10 (64.7%)	p < 0.001	p < 0.001

Intragroup p values determined by t-test, Intergroup values determined by Mann Whitney U 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	0/8 (0%)	0/25 (0%)	0/7 (0%)	7/25 (28.0%)
Day 60	0/8 (0%)	7/25 (28.0%)	1/7 (14.3%)	20/24 (83.3%)
Day 90	0/8 (0%)	8/24 (33.3%)	4/7 (57.1%)	23/24 (95.8%)

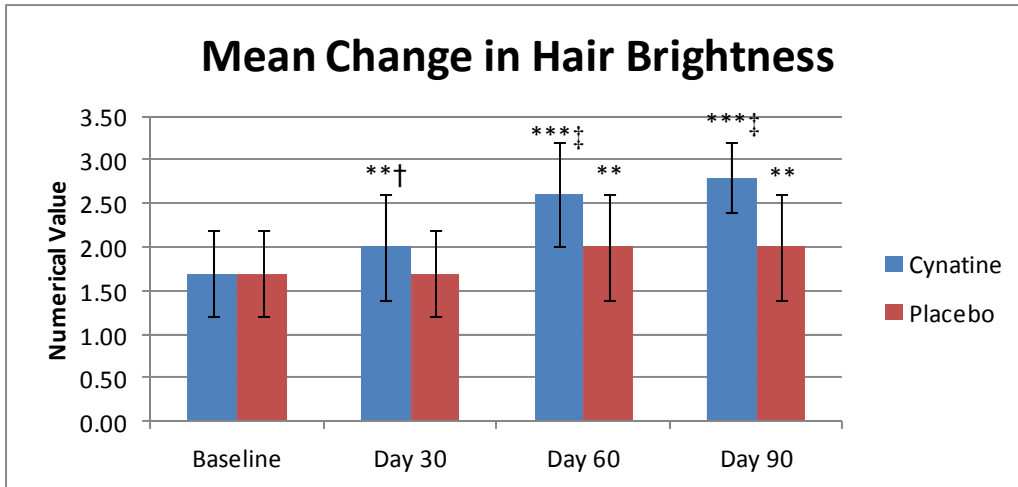
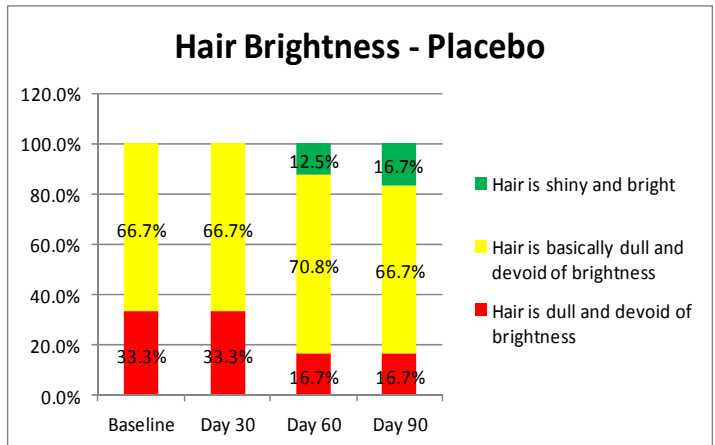
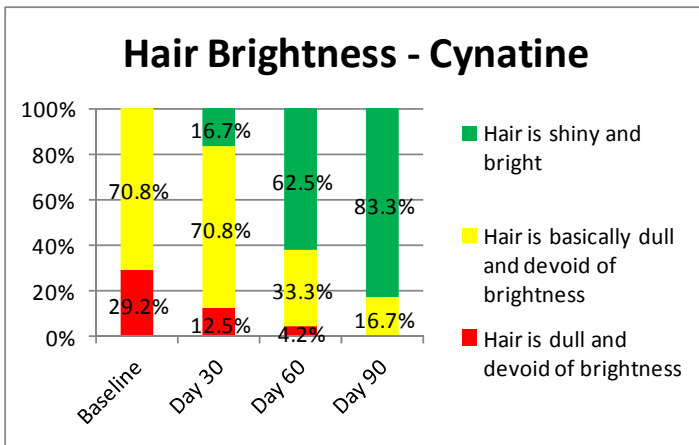


Figure 9. Hair brightness results for Cynatine and Placebo.
 * p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.02, ‡ p <0.001 between groups to baseline



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 95% of subjects on Cynatine had at least a 1 unit increase in the look of their hair, where as less than 35% had the same effect on placebo
- Of the subjects which started with a hair score of 1 (allowing for 2 units of improvement) over 50% 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

2. Evaluation of Cynatine on Skin

This section looks at 6 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.
- It should be noted that this clinical was performed in the winter when the skin generally loses moisture

Table 12. Analyses (Skin– Moisturization)

Moisturization	Study Group				
	Placebo		Cynatine® HNS		p-value between groups
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	
Baseline	42.0 ± 4.6		41.9 ± 4.1		
Day 30	38.4 ± 5.2		44.0 ± 5.9		
Day 60	36.2 ± 4.4		45.3 ± 6.4		
Day 90	33.5 ± 4.0		46.2 ± 5.5		
<u>Change to Baseline:</u>					
Day 30	-3.6 (-7.9%)	p < 0.01	2.1 (5.4%)	p < 0.05	P < 0.01
Day 60	-5.8 (-12.9%)	p < 0.001	3.4 (9.3%)	p < 0.05	p < 0.001
Day 90	-8.5 (-19.3%)	p < 0.001	4.3 (11.1%)	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 13. % Responders

	Placebo		Cynatine® HNS	
	Responders >0%	Responders <0%	Responders > 0%	Responders < 0%
Day 30	10/25 (40.0%)	15/25 (60.0%)	14/25 (56.0%)	11/25 (44.0%)
Day 60	4/25 (16.0%)	21/25 (84.0%)	14/24 (58.3%)	10/24 (41.7%)
Day 90	2/24 (8.3%)	22/24 (91.7%)	19/24 (79.2%)	5/24 (20.8%)

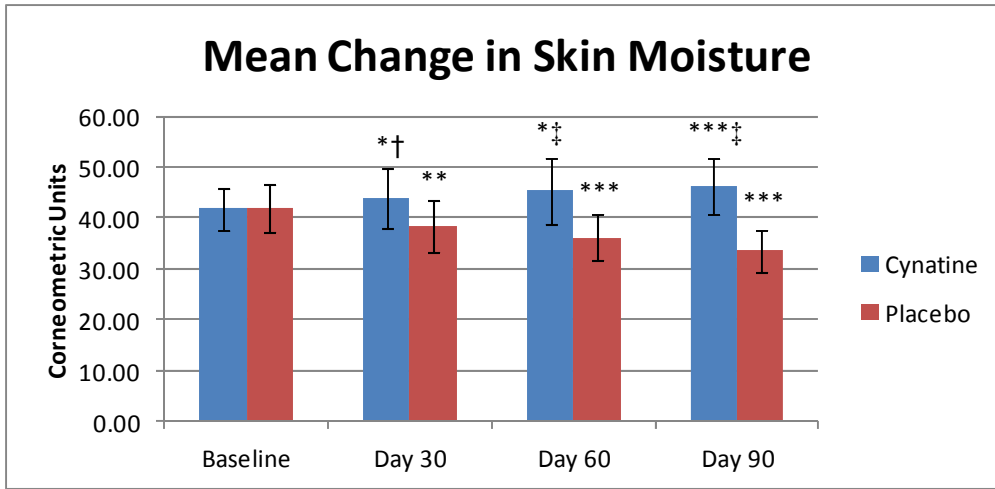


Figure 12. Mean change in skin moisture for Cynatine and Placebo.
 *p < 0.05, ** p < 0.01, ***p < 0.001 within group to baseline,
 † p < 0.01, ‡ p < 0.001 between groups to baseline

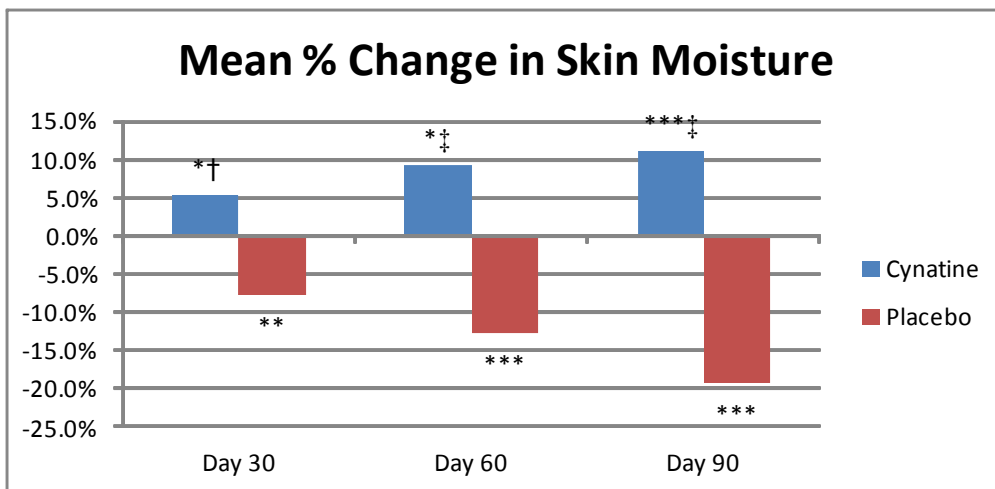


Figure 13. Mean % change in skin moisture for Cynatine and Placebo.
 *p < 0.05, ** p < 0.01, ***p < 0.001 within group to baseline,
 † p < 0.01, ‡ p < 0.001 between groups to baseline

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
- Almost 80% of subjects on Cynatine had at least an increase in skin moisture at 90 days, whereas less than 10% had the same effect on placebo
- Cynatine increased skin moisture over placebo by over 30%

Structure Function Claims:

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

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		p-value between groups
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	
Baseline	0.6910 ± 0.0761		0.6819 ± 0.0680		
Day 30	0.6751 ± 0.0890		0.7106 ± 0.0972		
Day 60	0.6688 ± 0.0916		0.7268 ± 0.0719		
Day 90	0.6593 ± 0.0893		0.7614 ± 0.0851		
<u>Change to Baseline:</u>					
Day 30	-0.0159 (-2.3%)	p <0.05	0.0287 (4.3%)	p <0.05	n.s.
Day 60	-0.0222 (-3.2%)	P <0.05	0.0449 (7.2%)	p < 0.01	p < 0.01
Day 90	-0.0317 (-4.6%)	p < 0.01	0.0795 (12.2%)	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 >0%	Responders <0%	Responders > 0%	Responders < 0%
Day 30	10/25 (40.0%)	15/25 (60.0%)	20/25 (80.0%)	5/25 (20.0%)
Day 60	8/25 (32.0%)	17/25 (68.0%)	19/24 (79.2%)	5/24 (20.8%)
Day 90	9/24 (37.5%)	15/24 (62.5%)	21/24 (87.5%)	3/24 (12.5%)

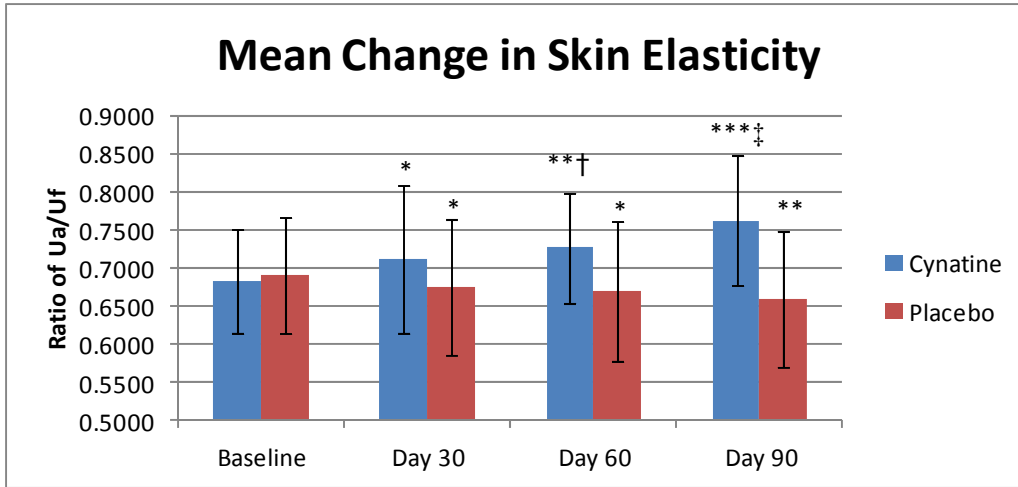


Figure 14. Mean Change in Skin Elasticity for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.01, ‡ p <0.001 between groups to baseline

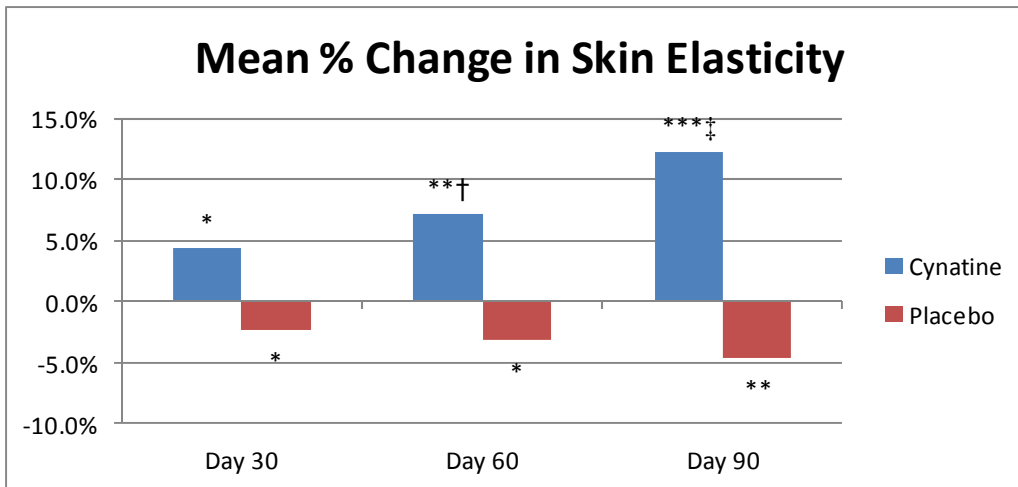


Figure 15. Mean % Change in Skin Elasticity for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.01, ‡ p <0.001 between groups to baseline

Conclusion:

- Cynatine increases the elasticity of skin after 60 days
- Cynatine showed results that were statistically significant to both baseline and placebo at 60 and 90 days
- 80% of subjects on Cynatine had at least an increase in skin elasticity at 30 days, where as 40% had the same effect on placebo, this trend continued over the 60 and 90 day time periods
- Cynatine increased skin elasticity over placebo by over 16% at 90 days

Structure Function Claims:

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

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 Ra parameter (skin smoothness), the Rz parameter (skin roughness) and the wrinkle depth.

Table 16. Analyses (Skin– Smoothness Ra Parameter)

Smoothness	Study Group				
	Placebo		Cynatine [®] HNS		p-value between groups
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	
Baseline	35.9 ± 3.2		35.5 ± 3.4		
Day 30	36.0 ± 3.1		33.9 ± 5.4		
Day 60	36.6 ± 3.5		33.0 ± 4.3		
Day 90	38.6 ± 4.7		32.0 ± 4.4		
<u>Change to Base-line:</u>					
Day 30	0.1 (0.3%)	n.s.	-1.6 (-4.7%)	p < 0.05	n.s.
Day 60	0.7 (2.1%)	n.s.	-2.5 (-7.3%)	p < 0.001	p < 0.01
Day 90	2.7 (7.8%)	p < 0.01	-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	16/25 (64.0%)	9/25 (36.0%)	10/25 (40.0%)	15/25 (60.0%)
Day 60	17/25 (68.0%)	8/25 (32.0%)	6/24 (25.0%)	18/24 (75.0%)
Day 90	18/24 (70.8%)	7/24 (29.2%)	5/24 (20.8%)	19/24 (79.2%)

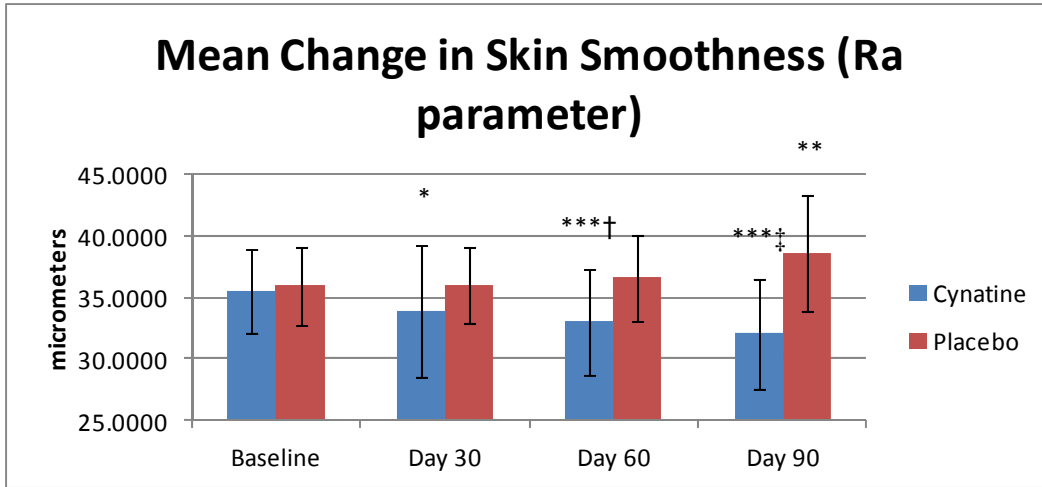


Figure 16. Mean change in skin smoothness for Cynatine and Placebo.

*p <0.05, ** p<0.01, ***p<0.001 within group to baseline, † p <0.01, ‡ p <0.001 between groups to baseline

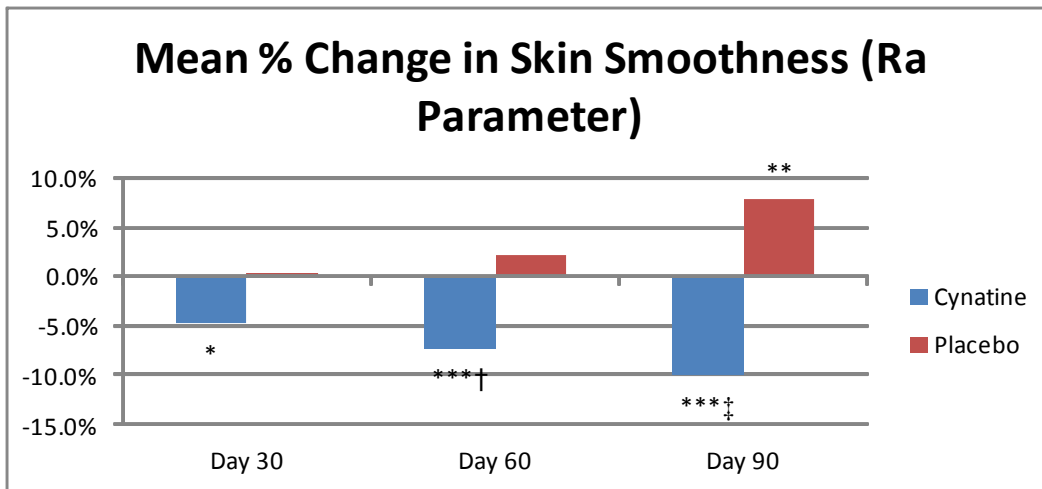


Figure 17. Mean % change in skin smoothness for Cynatine and Placebo.

*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		p-value between groups
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	
Baseline	139.6 ± 14.5		136.0 ± 14.7		
Day 30	140.6 ± 16.0		132.1 ± 13.0		
Day 60	141.3 ± 15.8		126.6 ± 11.5		
Day 90	139.8 ± 17.3		123.6 ± 12.7		
<u>Change to Baseline:</u>					
Day 30	1.0 (0.8%)	n.s.	-3.9 (-2.6%)	p <0.05	n.s.
Day 60	1.7 (1.5%)	n.s.	-9.4 (-6.5%)	p < 0.001	p < 0.001
Day 90	0.2 (0.3%)	n.s.	-12.4 (-8.6%)	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 19. % Responders (skin roughness)

	Placebo		Cynatine [®] HNS	
	Responders >0%	Responders <0%	Responders > 0%	Responders < 0%
Day 30	12/25 (48.0%)	13/25 (52.0%)	11/25 (44.0%)	14/25 (56.0%)
Day 60	13/25 (52.0%)	12/25 (48.0%)	6/24 (25.0%)	18/24 (75.0%)
Day 90	11/24 (45.8%)	13/24 (54.2%)	5/24 (20.8%)	19/24 (79.2%)

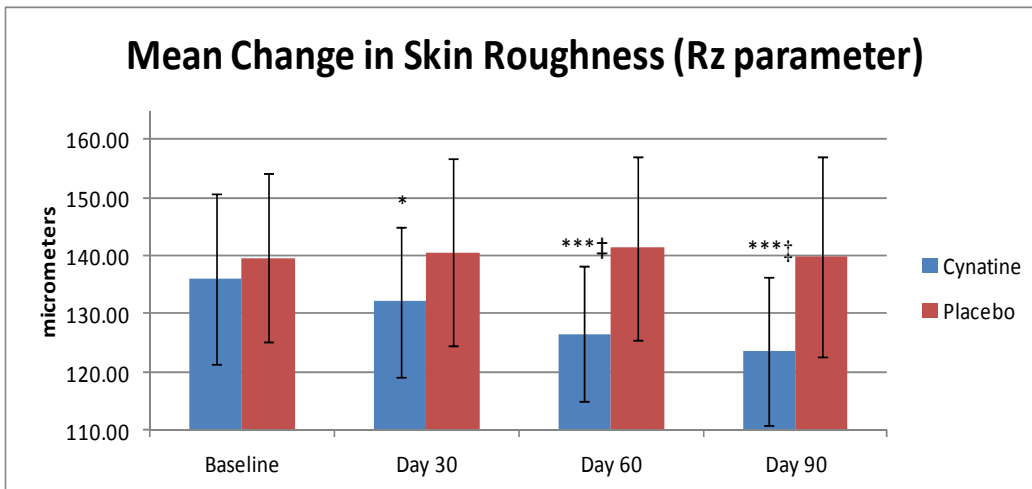


Figure 18. Mean Change in Skin roughness for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

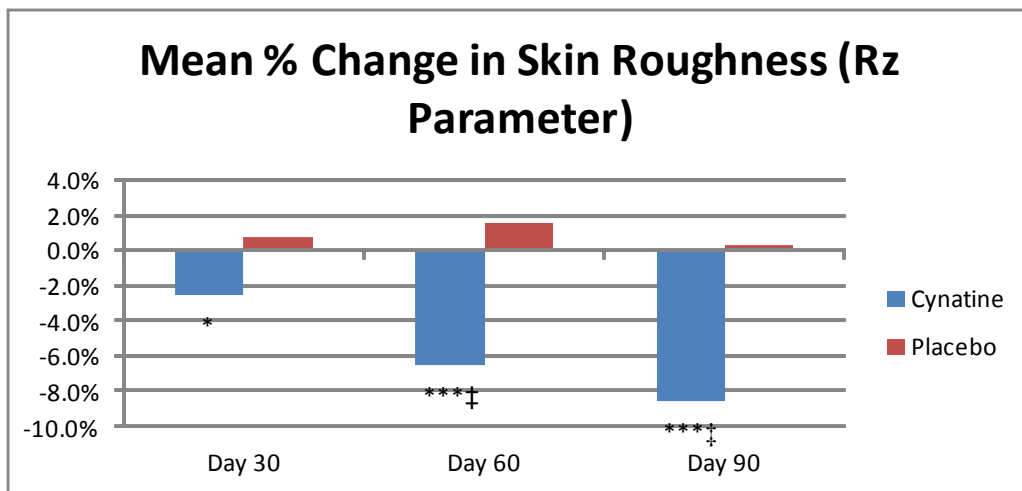


Figure 19. Mean Change in Skin roughness for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

Table 20. Analyses (Skin– Wrinkle Depth)

Wrinkle Depth	Study Group				
	Placebo		Cynatine® HNS		p-value between groups
	Mean ± SD	p-value (v. Baseline)	Mean ± SD	p-value (v. Baseline)	
Baseline	460.4 ± 62.9		451.9 ± 61.3		
Day 30	457.0 ± 55.6		436.5 ± 56.4		
Day 60	462.4 ± 56.8		412.2 ± 47.6		
Day 90	458.4 ± 61.6		397.6 ± 53.9		
<u>Change to Baseline:</u>					
Day 30	-3.4 (-0.5%)	n.s.	-15.4 (-3.1%)	p < 0.05	n.s.
Day 60	2.0 (0.8%)	n.s.	-39.7 (-8.3%)	p < 0.001	p < 0.001
Day 90	-2.0 (-0.2%)	n.s.	-54.3 (-11.5%)	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	13/25 (52.0%)	12/25 (48.0%)	12/25 (48.0%)	13/25 (52.0%)
Day 60	13/25 (52.0%)	12/25 (48.0%)	5/24 (20.8%)	19/24 (79.2%)
Day 90	11/24 (45.8%)	13/24 (54.2%)	6/24 (25.0%)	18/24 (75.0%)

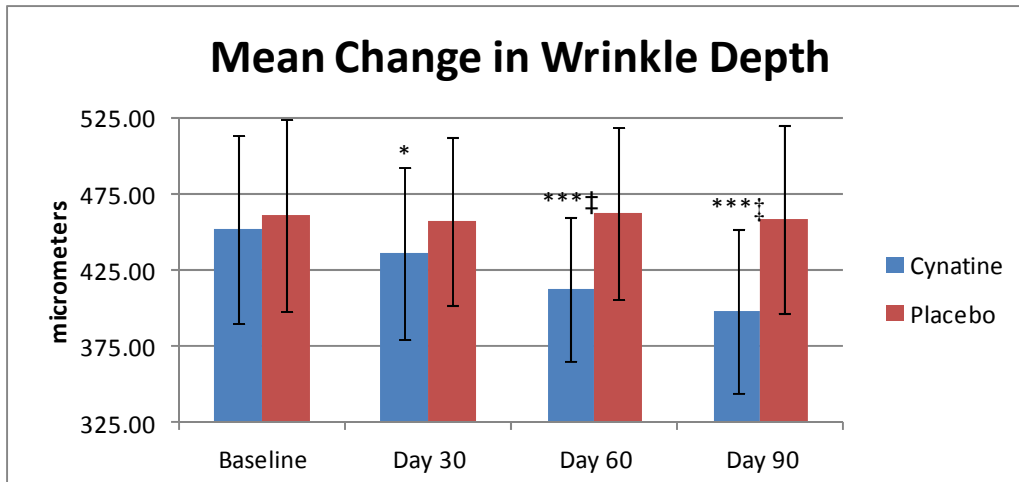


Figure 20. Mean change in wrinkle depth for Cynatine and Placebo. *p < 0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p < 0.001 between groups to baseline

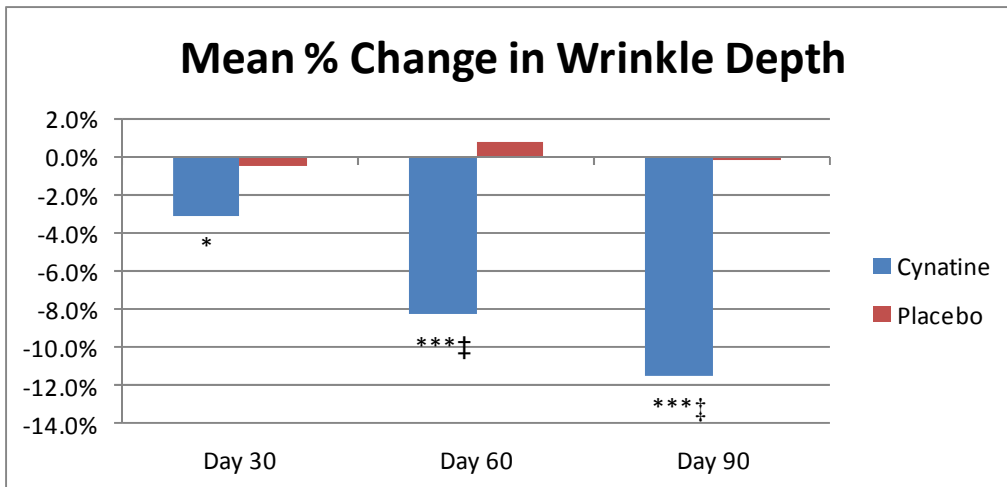


Figure 21. Mean % change in wrinkle depth for Cynatine and Placebo. *p <0.05, ** p<0.01, ***p<0.001 within group to baseline, ‡ p <0.001 between groups to baseline

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 75% 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 60% of subjects on Cynatine at 30 days and improves to almost 80% by 90 Days, while placebo peaks at 36% at 30 days and decreases at each further time point
- Cynatine decreases skin wrinkles over placebo by approximately 9 to 18% 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.

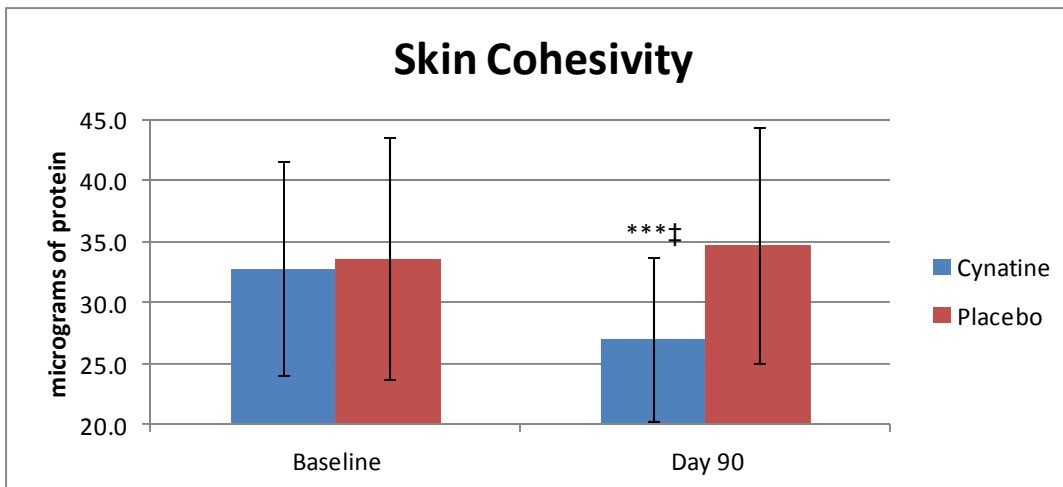
Table 22. Analyses (Skin– Cohesivity Protein Content)

Protein Content	Study Group		
	Placebo	Cynatine® HNS	
	Mean ± SD	Mean ± SD	p-value between groups
Baseline	33.6 ± 6.3	32.8 ± 8.7	
Day 90	34.7 ± 7.0	27.0 ± 6.7	
<u>Change to Baseline:</u>			
Day 90	0.9 (3.8%)	-5.8 (-15.9%)	p < 0.001
(Min,Max)	(26.1%, -13.2%)	(1.5%, -55.1%)	
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

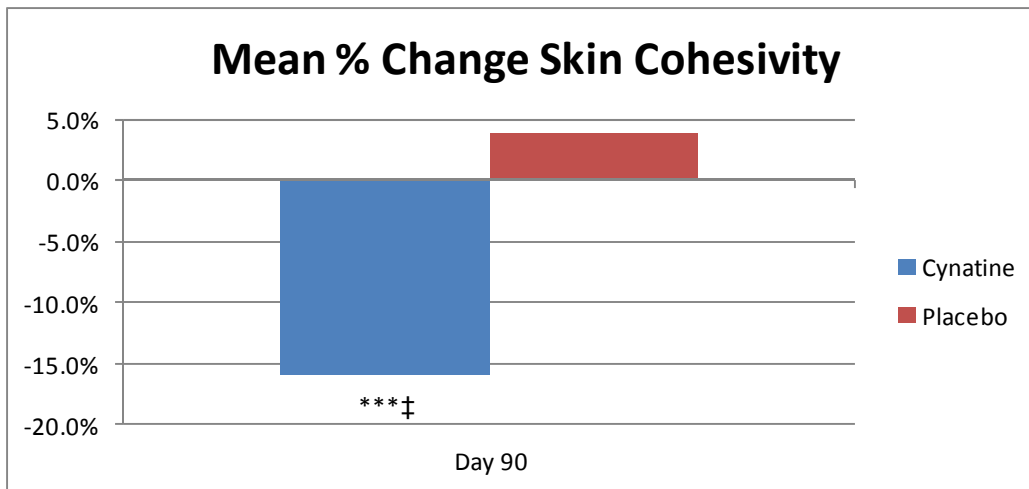
Table 23. % Responders

	Placebo		Cynatine® HNS	
	Responders >0%	Responders <0%	Responders >0%	Responders <0%
Day 90	13/24 (54.2%)	11/24 (45.8%)	1/24 (4.2%)	23/24 (95.8%)



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

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

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

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	2.3	2.2	
<u>Change to Base-line:</u>			
Day 30	1.0 ± 0.0	1.9 ± 0.7	p < 0.001
Day 60	1.1 ± 0.4	2.2 ± 0.8	p <0.001
Day 90	1.3 ± 0.5	2.7 ± 1.0	p <0.001

Intergroup p values determined by Two Sided Mann Whitney U Test, p <0.05 is significant

Table 25. % Responders

	Placebo		Cynatine® HNS	
	Responders > 1	Responders 1	Responders > 1	Responders 1
Day 90	4/14 (28.5%)	11/24 (71.5%)	14/16 (87.5%)	2/16 (12.5%)

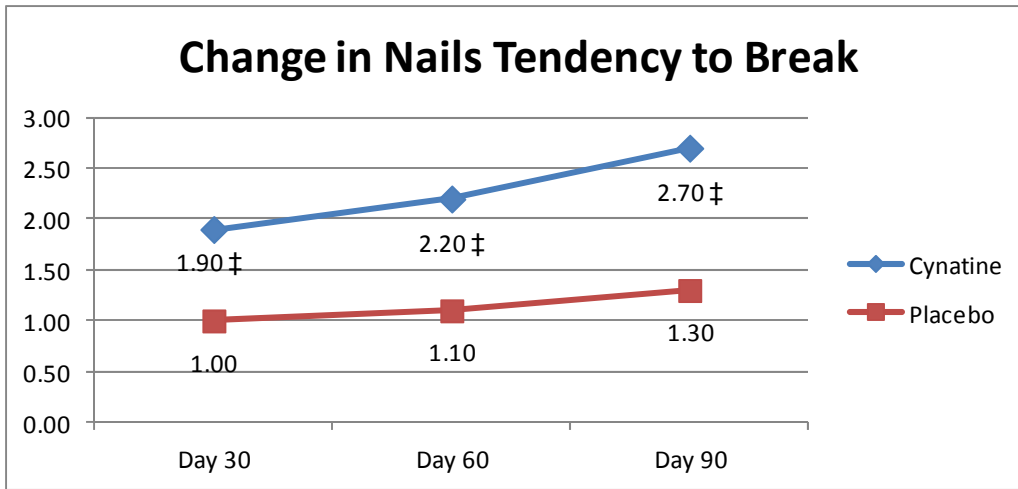


Figure 24. Change in Nails Tendency to Break for Cynatine and Placebo.
‡ p <0.001 between groups to baseline

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 87% 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

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%

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	37.5%	79.2%	83.3%	87.5%	41.7%	<0.01	45.8%	<0.01	50%	<0.01
	Soft	62.5%	20.8%	16.7%	12.5%						
Placebo	Hard	41.7%	50%	54.2%	58.3%	8.3%		12.5%		16.7%	
	Soft	58.3%	50%	45.8%	41.7%						
Cynatine HNS	Resistant	33.3%	75.0%	79.2%	87.5%	41.7%	<0.01	45.8%	<0.01	54.2%	<0.01
	Fragile	66.7%	25.0%	20.8%	12.5%						
Placebo	Resistant	41.7%	50%	54.2%	58.3%	8.3%		12.5%		16.7%	
	Fragile	58.3%	50%	45.8%	41.7%						
Cynatine HNS	Broken	45.8%	25.0%	16.7%	12.5%						
	Not Broken	54.2%	75.0%	83.3%	87.5%	20.8%	<0.02	29.2%	<0.01	33.3%	<0.02
Placebo	Broken	50%	50%	45.8%	41.7%						
	Not Broken	50%	50%	54.2%	58.3%	0%		4.2%		8.3%	
Cynatine HNS	Rough	37.5%	25%	0%	0%						
	Smooth	62.5%	75%	100%	100%	12.5%	n.s.	37.5%	<0.01	37.5%	<0.01
Placebo	Rough	33.3%	33.3%	25%	20.8%						
	Smooth	66.7%	66.7%	75%	79.2%	0%		8.3%		12.5%	
Cynatine HNS	Yellowish	20.8%	20.8%	0%	0%						
	White (natural color)	79.2%	79.2%	100%	100%	0%	n.s.	20.8%	<0.05	20.8%	<0.01
Placebo	Yellowish	16.7%	12.5%	12.5%	12.5%						
	White (natural color)	83.3%	87.5%	87.5%	87.5%	4.2%		4.2%		4.2%	

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 was one dropout in both the Active and Placebo groups of the study which were both deemed to be not a result of the product taken by the medical examiner. 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:

Population:	50 women (25 active, 25 placebo)
Randomization:	Randomized, double blinded placebo control study
Study time:	December 2011 through March 2012
Location:	Farcoderm (University of Pavia), Italy