CYNATINE®
HNS

Technical Summary of Cynatine® HNS Clinical Trial 2019/0892

Study performed by : Complife Italia S.r.l;
Record number E.HU.016-0100-01-004L_2019/0892

Study design

Double blind Placebo controlled clinical study carried out on 50 male and 50 female subjects aimed at evaluating the efficacy of a food supplement, Cynatine® HNS, to help improve the conditions of skin, hair and nail.

1. EVALUATION OF CYNATINE® HNS ON HAIR

To evaluate its effect on hair 5 different tests have been used.

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 hair in three areas of the scalp and the total number of hair extracted is counted.
Healthy hair in the anagen phase should remained rooted, while hair in the telogen phase should be removed.
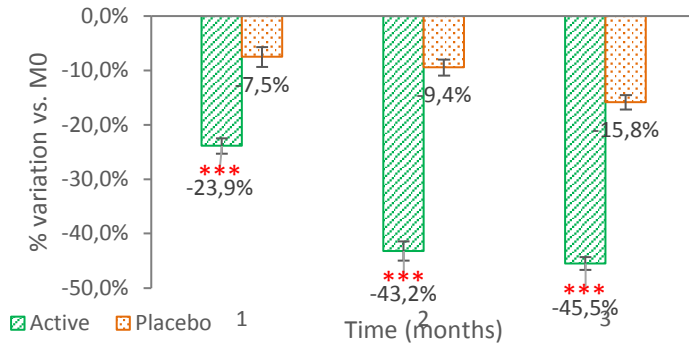
Table 1. Analyses (Hair- Pull Test) on overall subjects

Pull Test Score	Study Group Overall (male + female subjects)		
	Cynatine® HNS group Mean ± SD	Placebo group Mean ± SD	p-value intergroup (Cynatine® HNS vs. Placebo)
Baseline	12,9 ± 0,3	13,0 ± 0,3	
Day 30	9,8 ± 0,2	11,9 ± 0,3	
Day 60	7,2 ± 0,2	11,6 ± 0,2	
Day 90	6,9 ± 0,1	10,9 ± 0,2	
Change to Baseline (%):			
Day 30	-23,9%	-7,5%	p < 0,001
Day 60	-43,2%	-9,4%	p < 0,001
Day 90	-45,5%	-15,8%	p < 0,001

Intergroup values determined by t-test of Student, p < 0.05 are significant

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Figure 1. : hair Pull Test for overall subjects; mean % reduction from baseline for Cynatine® HNS and Placebo.
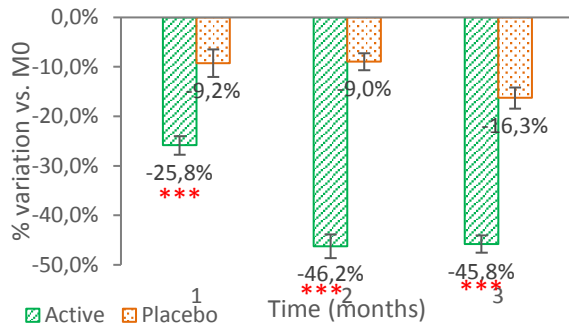

*** p < 0.001 between groups to baseline

Table 2. Analyses (Hair- Pull Test) on female and male subjects

| Pull Test Score | Study Groups | | | | | |
| | female subjects | | | male subjects | | |
	Cynatine group Mean ± SD	Placebo group ± SD Mean	p-value (Cynatine® HNS vs. Placebo)	Cynatine group Mean ± SD	Placebo group ± SD Mean	p-value (Cynatine® HNS vs. Placebo)
Baseline	13,1 ± 0,4	12,8 ± 0.3		12,8 ± 0,4	13,2 ± 0,4	
Day 30	9,6 ± 0,3	11,5 ± 0,4		9,9 ± 0,3	12,4 ± 0,4	
Day 60	6,9 ± 0,3	11,5 ± 0,2		7,5 ± 0,2	11,8 ± 0,3	
Day 90	7,0 ± 0,2	10,6 ± 0,3		6,9 ± 0,1	11,1 ± 0,3	
Change to Baseline (%):						
Day 30	-25,8%	-9,2%	p < 0,001	-21,9%	-5,7%	p <0,001
Day 60	-46,2%	-9,0%	p < 0,001	-40,1%	-9,9%	p <0,001
Day 90	-45,8%	-16,3%	p < 0,001	-45,2%	-15,4%	p <0,001

Intergroup values determined by t-test of Student, p < 0.05 are significant
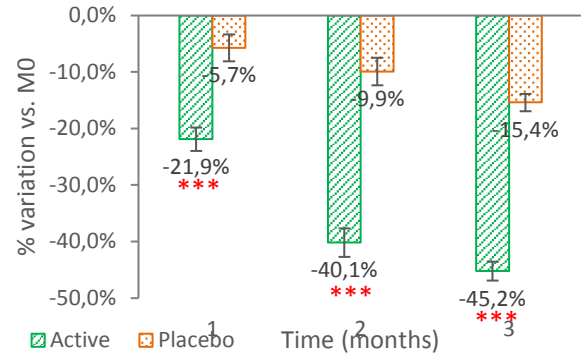
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Fig. 2a: Hair pull test for female subjects; mean % reduction from baseline for Cynatine® HNS and Placebo

Fig. 2b: Hair pull test for male subjects; mean % reduction from baseline for Cynatine® HNS and Placebo

*** p < 0.001 between groups to baseline

Conclusion for overall population and in female and male groups:

- Cynatine® HNS reduced hair loss around 3 times more than Placebo at 30, 60 and 90 days.
- Cynatine® HNS showed a statistically significant decrease in hair loss vs. Placebo at 30, 60 and 90 days with p value < 0.001.

Possible Structure Function Claims:

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

b. Anagen/Telogen Phase Hair Test

In order to measure the number of hair 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.

Computer software then analyzed the two pictures and could determine how many hair were growing (Anagen phase) and how many hair died (Telogen phase).
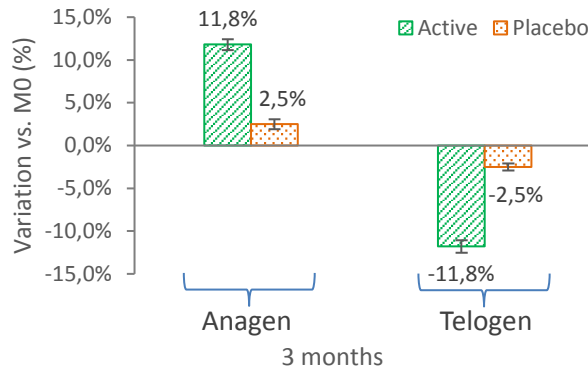
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Table 3. Analyses (Hair– Anagen/Telogen Phase) on overall subjects:

| Anagen / Telogen score | Study Group Overall (male + female subjects) | | | | p-value (Cynatine® HNS vs. Placebo) |
| | Cynatine® HNS group Mean ± SD | | Placebo group Mean ± SD | | |
	Anagen	Telogen	Anagen	Telogen	
Baseline Day 90	72,3% ± 0,1 84,1% ± 0,2	27,7% ± 0,1 15,9% ± 0,2	72,8% ± 0,1 75,3% ± 0,1	27,2% ± 0,1 24,7% ± 0,1	
Change to Baseline (%): Day 90	+11,8%	-11,8%	+2,5%	-2,5%	p < 0,001

Intergroup values determined by t-test of Student, p < 0.05 are significant.

Figure 3: for overall subjects; mean % change in hair in the Anagen and Telogen phase for CYNATINE® HNS and Placebo.

*** p < 0.001 between groups to baseline

Table 4. Analyses (Hair– Anagen/Telogen Phase) on female and male subjects

| Anagen / Telogen score | female subjects | | | | | male subjects | | | | |
| | Cynatine® HNS group Mean ± SD | | Placebo group Mean ± SD | | p-value (active vs. Placebo) | Cynatine® HNS group Mean ± SD | | Placebo group Mean ± SD | | p-value (active vs. Placebo) |
	Anagen	Telogen	Anagen	Telogen		Anagen	Telogen	Anagen	Telogen	
Baseline	72,9% ± 0,2	27,1% ± 0,2	73.0% ± 0.1	27.0% ± 0,1		71,8% ± 0,2	28,2% ± 0,2	72,7% ± 0,2	27.3% ± 0,2	
Day 90	85,3% ± 0,2	14,7% ± 0,2	75.5% ± 0,1	24,5% ± 0,1		82.9% ± 0,2	17.1% ± 0,2	75.1% ± 0,1	24,9% ± 0,1	
Change to Baseline (%): Day 90	+12,4%	-12,4%	+2,5%	-2,5%	p < 0,001	+11,1%	-11,1%	+2,4%	-2,4%	p < 0,001

Intergroup values determined by t-test of Student, p < 0.05 are significant.

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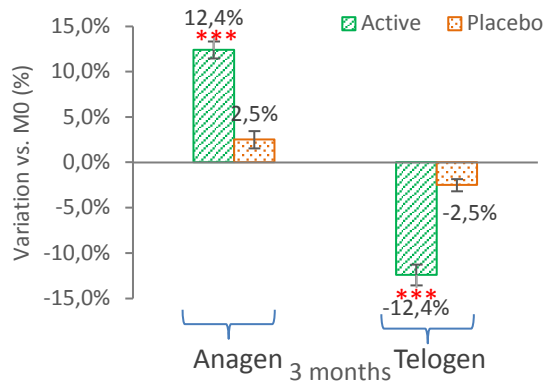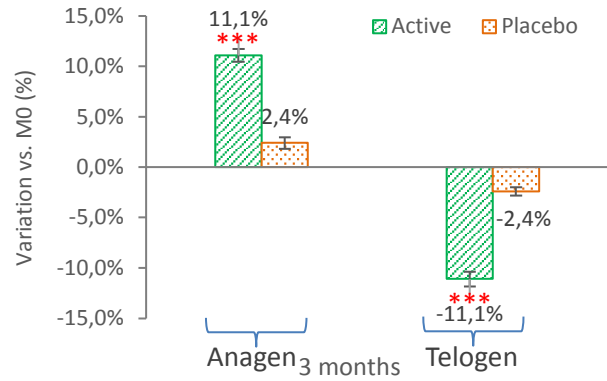Fig. 4a: Female subjects, mean % change in hair anagen/ telogen phase

Fig. 4b: Male subjects, mean % change in hair anagen/ telogen phase

*** p < 0.001 between groups to baseline

Conclusion for overall population and in female and male groups:

- Cynatine® HNS increases the number of hair in the Anagen phase and reduces the number of hair in Telogen phase after 90 days.
- Cynatine® HNS vs. Placebo showed results that were statistically very significant at 90 days on the global population as well as on men and women.
- Cynatine® HNS's effect over Placebo was greater than 4.5 times more for all groups.

Possible Structure Function Claims:
- Cynatine® HNS supports healthy hair growth.

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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 quantities of the important amino acids which play a role in hair health (Serine,Glutamic Acid, Cystine and Methionine) have been measured below:

Table 5. Analyses on overall population (Hair– Amino Acid)

Amino Acid Score	Study Group Overall								p value between groups (Cynatine® HNS vs. Placebo) :
	Cynatine® HNS				Placebo				
	Serine	Glutamic Acid	Cystine	Methionine	Serine	Glutamic Acid	Cystine	Methionine	
	Mean % ± SD %				Mean % ± SD %				
Baseline	11,0 ± 0,4	14,3 ± 0,4	17,4 ± 0,4	1,1 ± 0,1	11,3 ± 0,4	13,9 ± 0,5	17,8 ± 0,5	1,2 ± 0,1	
Day 90	15,4 ± 0,5	18,1 ± 0,4	26,8 ± 0,6	4,7 ± 0,2	11,7 ± 0,3	14,1 ± 0,5	16,9 ± 0,4	1,2 ± 0,1	
Change to Baseline:									for all values p < 0,001
Day 90	+4,5%	+3,8%	+9,4%	+3,6%	+0,4%	+0,2%	-0,8%	+0,0%	
p value (vs. baseline)	p < 0,001	p < 0,001	p < 0,001	p < 0,001	n.s.	n.s.	n.s.	n.s.	

Intragroup and intergroup values determined by RM-ANOVA and t-test of Student, p < 0.05 are significant.
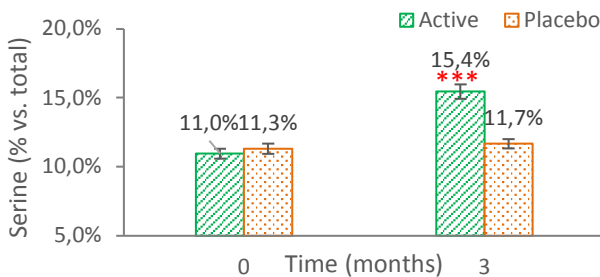
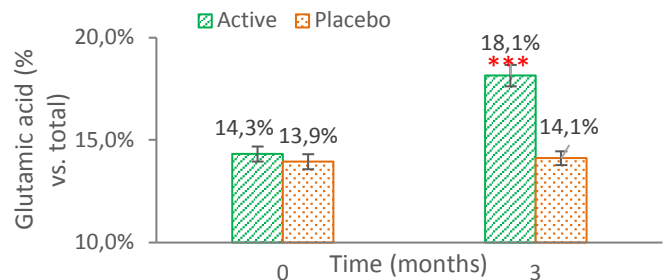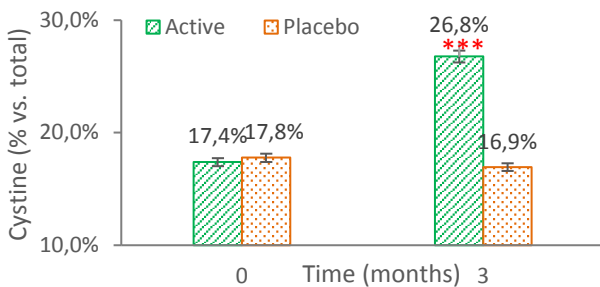Fig. 5a: Serine content
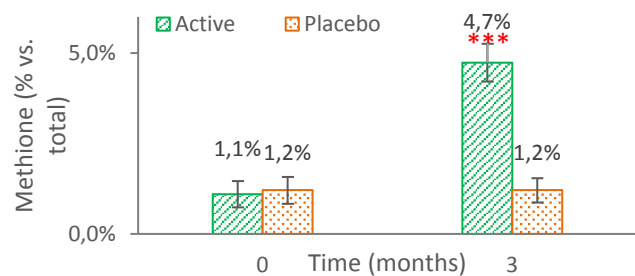

Fig 5b: Glutamic acid content

Fig. 5c: Cystine content

Fig. 5d: Methionine content

*** p < 0.001 for all amino acids content as variation vs M0 only in Cynatine® HNS group.

Fig. 5e: Mean % change in amino acid profil after 90 days

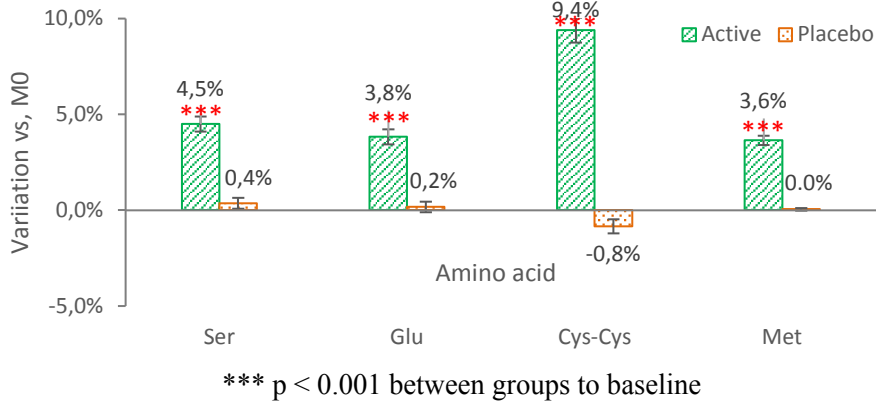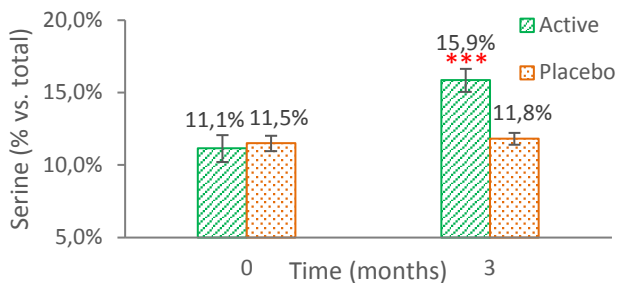*** p < 0.001 between groups to baseline

Table 6. Analyses on female subjects (Hair– Amino Acid)

Amino Acid Score	Study Group female subjects								p value between groups (Cynatine® HNS vs. Placebo) :
	Cynatine® HNS				Placebo				
	Serine	Glutamic Acid	Cystine	Methionine	Serine	Glutamic Acid	Cystine	Methionine	
	Mean % ± SD %				Mean % ± SD %				
Baseline	11,1 ± 0,6	14,5 ± 0,5	17,1 ± 0,5	1,1 ± 0,1	11,5 ± 0,5	14,0 ± 0,7	17,6 ± 0,6	1,2 ± 0,1	for all values p < 0,001
Day 90	15,9 ± 0,8	18,2 ± 0,6	27,0 ± 0,8	4,7 ± 0,3	11,8 ± 0,4	14,2 ± 0,8	16,9 ± 0,6	1,3 ± 0,1	
Change to Baseline: Day 90	+4,7%	+3.7%	+9,9%	+3.5%	+0,3%	+0,2%	-0,8%	0,1%	
p value (vs. baseline)	p < 0,001	p < 0,001	p < 0,001	p < 0,001	n.s.	n.s.	n.s.	n.s.	

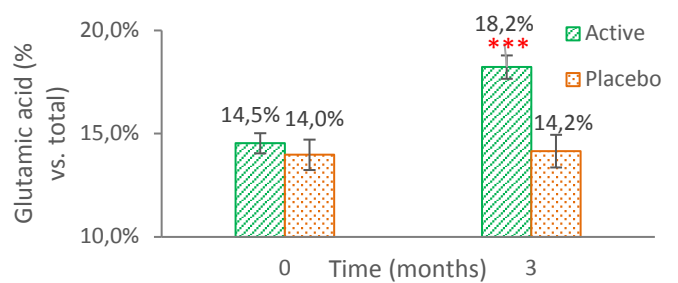Intragroup and intergroup values determined by RM-ANOVA and t-test of Student, $p < 0.05$ are significant.

Fig. 6a: Serine content

Fig. 6b: Glutamic acid content
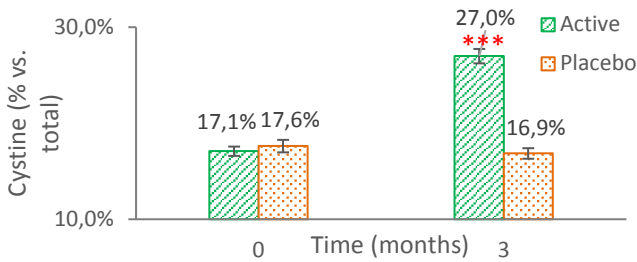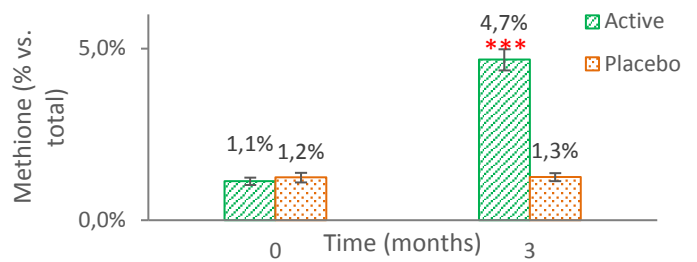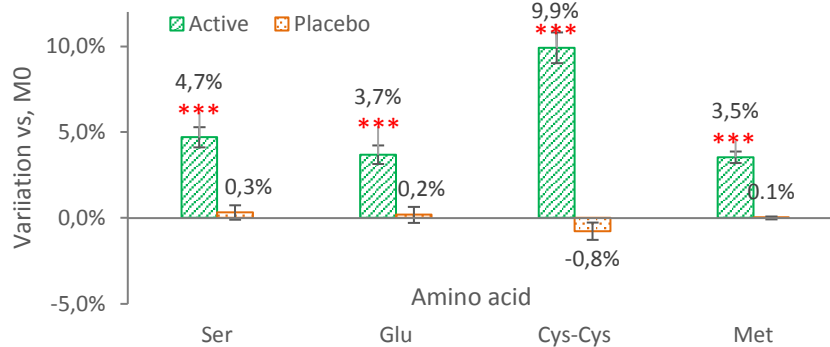
Fig. 6c: Cystine content

Fig. 6d: Methionine content

*** p < 0.001 for all amino acids content as variation vs M0 only in Cynatine® HNS group.

Fig. 6e: Female subjects mean % change in amino acid profile after 90 days

*** p < 0.001 between groups to baseline

Table 7. Analyses on male subjects (Hair– Amino Acid)

Amino Acid Score	Study Group male subjects								p value between groups (Cynatine® HNS vs. Placebo) :
	Cynatine® HNS				Placebo				
	Serine	Glutamic Acid	Cystine	Methionine	Serine	Glutamic Acid	Cystine	Methionine	
	Mean % ± SD %				Mean % ± SD %				
Baseline	10,8 ± 0,5	14,1 ± 0,6	17,7 ± 0,6	1,1 ± 0,1	11,1 ± 0,5	13,9 ± 0,6	17,9 ± 0,7	1,1 ± 0,1	
Day 90	15,0 ± 0,7	18,1 ± 0,6	26,6 ± 0,8	4,8 ± 0,3	11,5 ± 0,5	14,1 ± 0,7	17,0 ± 0,6	1,2 ± 0,1	for all values P < 0,001
Change to Baseline: Day 90	+4,3%	+4,0%	+8,9%	+3,7%	+0,4%	+0,2%	-0,9%	0,1%	
p value (vs. baseline)	p < 0,001	p < 0,001	p < 0,001	p < 0,001	n.s.	n.s.	n.s.	n.s.	

Intragroup and intergroup values determined by RM-ANOVA and t-test of Student, p < 0.05 are significant.

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37, Av du Mistral Athélia IV
13705 La Ciotat France
Tel: +(0)6 26 18 15 00 Fax +33 04 42 08 89 49 lcarlini@keratinnov.com   Page **8/30**

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Fig. 7a) Serine content
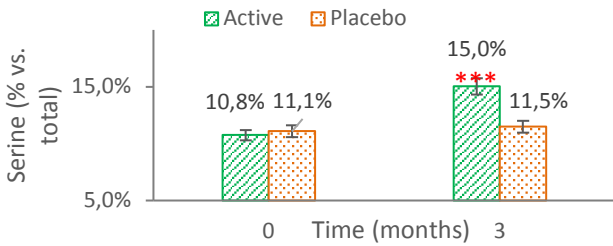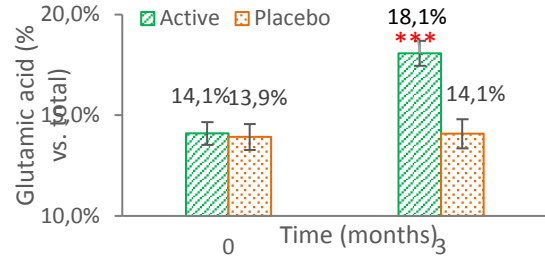

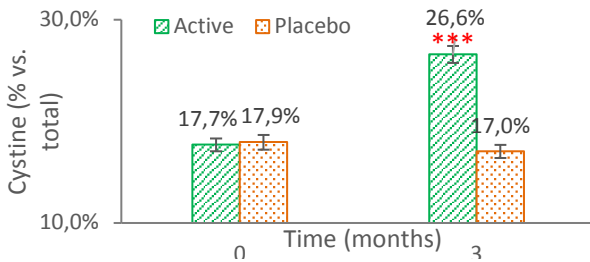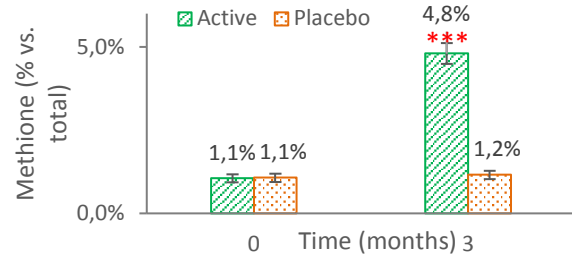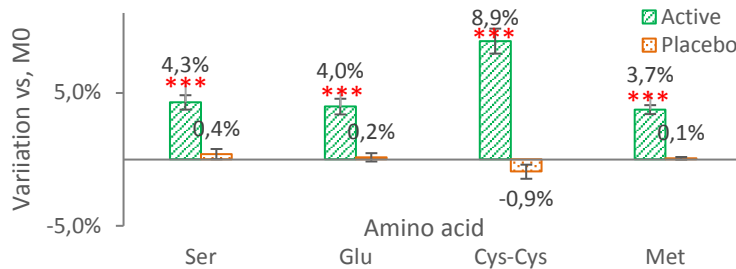Fig. 7b) Glutamic acid content

Fig 7c) Cystine content

Fig. 7d) Methionine content

$p < 0.001$ for all amino acids content as variation vs M0 only in Cynatine® HNS group.

Fig. 7e) Male subjects mean % change in amino acid profile after 90 days

*** $p < 0.001$ between groups to baseline

Conclusion for overall population and in female and male groups:

- Cynatine® HNS increases the amino acid content of Serine, Glutamic acid, Cystine and Methionine after 90 days.
- Cynatine® HNS showed results that were statistically significant versus baseline and versus Placebo at 90 days.
- The ability of the hair to absorb the amino acids from Cynatine® HNS shows its bioactivity.

Possible Structure Function Claims:

- Cynatine® HNS supports healthy hair growth.
- Cynatine® HNS improves the structure of the hair.
- Cynatine® HNS is bioactive.

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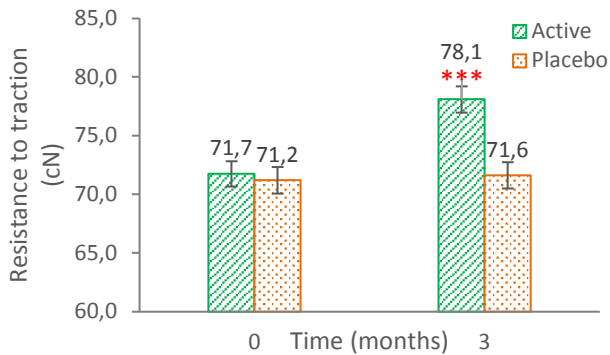
d. Resistance to Traction

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 on overall subjects (Hair– Resistance to Traction)

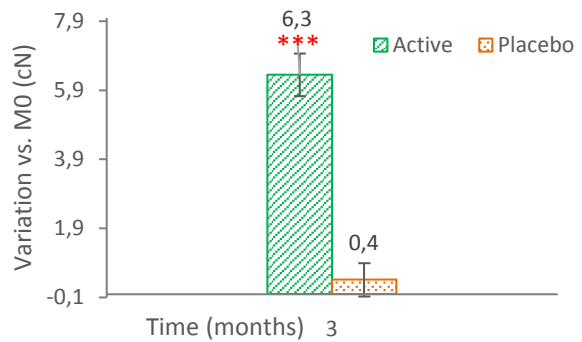| Resistance to traction score	Study Group Overall (male + female subjects)		p-value (Cynatine® HNS vs. Placebo)
	Cynatine® HNS group Mean ± SD	Placebo group Mean ± SD	
Baseline	71,7 cN ± 1,1	71,2 cN ± 1,1	
Day 90	78,1 cN ± 1,1	71,6 cN ± 1,1	
Change to Baseline (cN):			
Day 90	+6,3 cN	+0,4 cN	p < 0,001
p value (vs. baseline)	p < 0,001	n.s.	

Intragroup and intergroup values determined by RM-ANOVA and t-test of Student, p < 0.05 are significant.

Fig. 8a: Hair resistance to traction results for Cynatine® HNS and Placebo.

Fig. 8b: Mean variation vs. M0 in resistance to traction for Cynatine® HNS and Placebo.

*** p < 0.001 within group to baseline

*** p < 0.001 between groups to baseline

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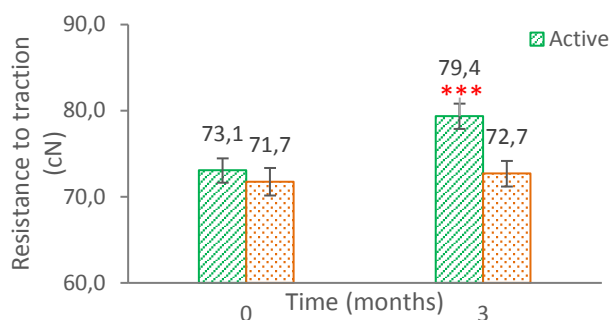
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Table 9. Analyses on female subjects (Hair– Resistance to Traction)

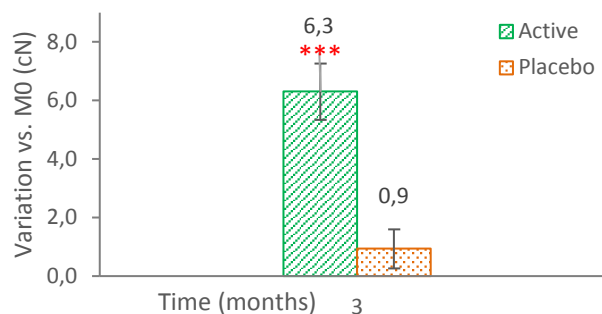| Resistance to traction score	Study Group female subjects		p-value (Cynatine® HNS vs. Placebo)
	Cynatine® HNS group Mean ± SD	Placebo group Mean ± SD	
Baseline	73,1 cN ± 1,4	71,7 cN ± 1,6	
Day 90	79,4 cN ± 1,5	72,7 cN ± 1,5	
Change to Baseline (cN):			
Day 90	+6,3 cN	+0,9 cN	$p < 0,001$
p value (vs. baseline)	$p < 0,001$	n.s.	

Intragroup and intergroup values determined by RM-ANOVA and t-test of Student, $p < 0.05$ are significant.

Fig. 9a: Female hair resistance to traction results for Cynatine® HNS and Placebo.

Figure 9b: Female subjects mean variation vs. M0 in resistance to traction for Cynatine® HNS and Placebo

*** $p < 0.001$ within group to baseline

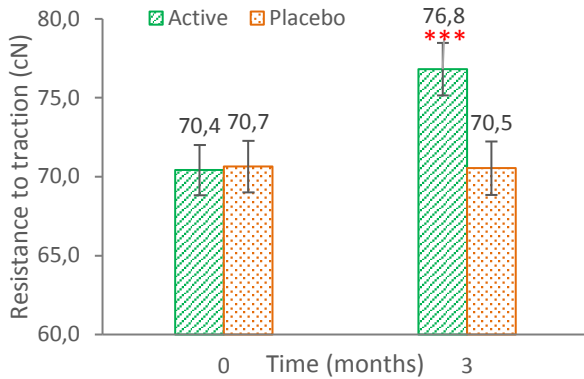*** $p < 0.001$ between groups to baseline

Table 10. Analyses on male subjects (Hair– Resistance to Traction)

Resistance to traction score	Study Group male subjects		p-value (Cynatine® HNS vs. Placebo)
	Cynatine® HNS group Mean ± SD	Placebo group Mean ± SD	
Baseline	70,4 cN ± 1,6	70,7 cN ± 1,6	
Day 90	76,8 cN ± 1,7	70,5 cN ± 1,7	
Change to Baseline (cN):			
Day 90	+6,4 cN	- 0,1 cN	$p < 0,001$
p value (vs. baseline)	$p < 0,001$	n.s.	

Intragroup and intergroup values determined by RM-ANOVA and t-test of Student, $p < 0.05$ are significant.
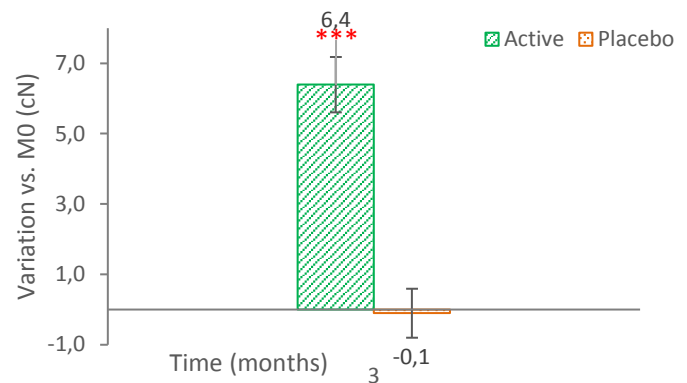
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Fig. 10a: Male subjects hair resistance to traction results for Cynatine® HNS and Placebo.

Fig. 10b: Male subjects mean variation vs. M0 in resistance to traction for Cynatine® HNS and Placebo.

*** p < 0.001 within group to baseline

*** p < 0.001 between groups to baseline

Conclusion for overall population and in female and male groups:

- Cynatine® HNS increases the strength of hair (approximately 9% in all groups) after 90 days.
- Cynatine® HNS showed results that were statistically very significant to both baseline and Placebo at 90 days.
- The demonstrated effect of Cynatine HNS is clearly superior to that demonstrated by the Placebo.

Possible Structure Function Claims:

- Cynatine® HNS supports healthy hair.
- Cynatine® HNS improves the structure of hair.
- Cynatine® HNS improves the strength of hair.

e. Hair Brightness Analysis

Cause of loss of hair brightness is the opening of the flakes and the loss of the hydrolipidic film. The dermatologist will evaluate it according to clinical scores.

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. Clinical classification of hair brightness is:

1 (Hair is dull and devoid of brightness).
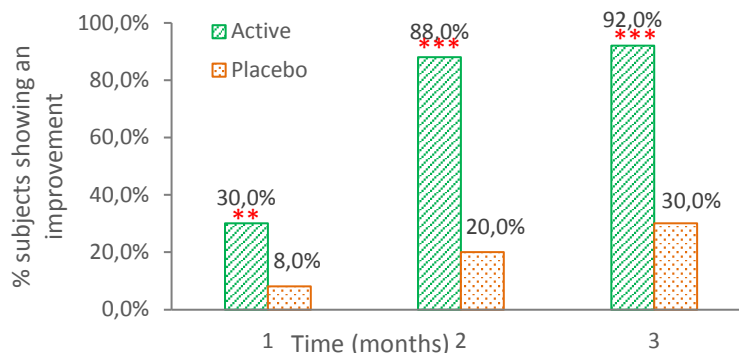2 (Hair is basically dull and not so bright)
3 (Hair is shiny and bright).

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Table 11. Analyses (Hair– Brightness Test) on overall population

Hair brightness score	Study Group overall (male + female subjects)		
	Cynatine® HNS group	Placebo group	p-value intergroup (Cynatine® HNS vs. Placebo)
Change to Baseline (%):			
Day 30	30%	8%	p<0,01
Day 60	88%	20%	p<0,001
Day 90	92%	30%	p<0,001

Intergroup determine by t-test of Student, values with p < 0.05 are significant.

Fig. 11: Mean % change in hair brightness for Cynatine® HNS and Placebo.

** p < 0.01, *** p < 0.001 between group to baseline

Table 12. Analyses (Hair brightness test) on female and male subjects

Hair brightness score	Study Group female subjects			Hair brightness score	Study Group male subjects		
	Cynatine® HNS group	Placebo group	p-value intergroup (Cynatine® HNS vs. Placebo)		Cynatine® HNS group	Placebo group	p-value intergroup (Cynatine® HNS vs. Placebo)
Change to Baseline (%):				Change to Baseline (%):			
Day 30	32%	8%	p<0,05	Day 30	28%	8%	n.s.
Day 60	88%	20%	p<0,001	Day 60	88%	20%	p<0,001
Day 90	92%	28%	p<0,001	Day 90	92%	32%	p<0,001

Intergroup determine by t-test of Student, values with p < 0.05 are significant.

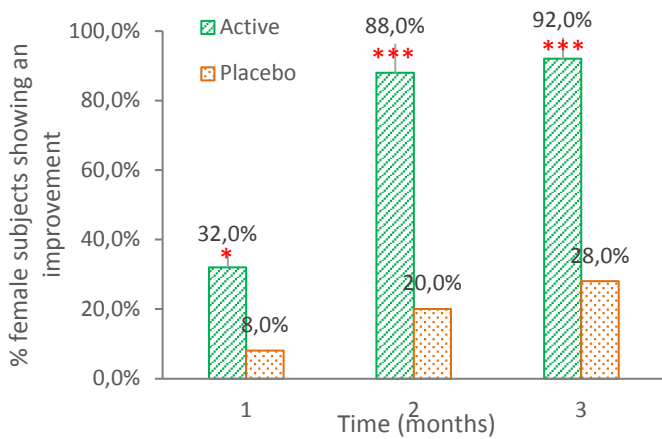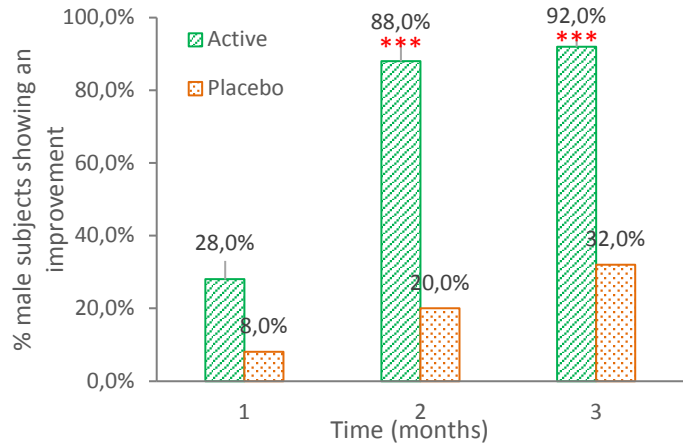Fig. 12a: Female subjects mean % change in hair brightness for Cynatine® HNS and Placebo.

Fig. 12b: Male subjects mean % change in hair brightness for Cynatine® HNS and Placebo.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ between group to baseline

Conclusion for overall population and in female and male groups:

- Cynatine® HNS increases the shine and brightness of hair after 30 days.
- Cynatine® HNS showed results that were statistically significant to the baseline and the Placebo at 30, 60 and 90 days.

Structure Function Claims:

- Cynatine® HNS supports healthy hair.
- Cynatine® HNS improves the shine and brightness of hair.

General conclusion on hair study:

This clinical study demonstrates the effect of Cynatine® HNS (500 mg/day) in improving hair conditions. The product was effective in improving hair conditions at all experimental monitored checkpoints. The variations obtained in the Cynatine® HNS group are statically significant from the variation obtained in the Placebo group

Product effects on the measured parameters were comparable between male and female subjects.

2. EVALUATION OF CYNATINE® HNS ON SKIN

Cynatine® HNS's effect on skin has been evaluated using 6 different tests.

a. Hydration and elasticity of the skin

The measurement of skin moisture is performed using the Internationally recognized CORNOMETER® method which measures the dielectric constant of water.

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 provide an analysis of the skin to return to its normal state after deformation stress.

Table 13. Analyses on overall population (Skin– Moisturization and elasticity)

Measured parameters	Overall population							
	Cynatine® HNS				Placebo			
	M0	M1	M2	M3	M0	M1	M2	M3
Skin moisturization	40,4% ± 1,1	42,8% ± 1,1	44,4% ± 1,1	45,5% ±1,1	39,5% ± 1,0	38,7% ± 0,9	38,4% ± 0,9	38,6% ± 0,9
Change to baseline %	-	+6,4%	+10,3%	+12,1%	-	-1,7%	-2,2%	-1,8%
p-value vs. Baseline	-	p<0,001	p<0,001	p<0,001	-	n.s	n.s.	n.s
Skin elasticity	0,7110 ± 0,0088	0,7415 ± 0,0088	0,7564 ± 0,0088	0,7831 ± 0,0088	0,7191 ± 0,0124	0,7207 ± 0,0114	0,7192 ± 0,0124	0,7375 ± 0,0128
Change to baseline %	-	+4,4%	+6,5%	+10,3%	-	+0,4%	+0,1%	+2,7%
p-value vs. Baseline	-	p<0,001	p<0,001	p<0,001	-	n.s	n.s	n.s.

values with $p < 0.05$ are significant.

Fig. 13a: mean % of skin moisture improvement from baseline for Cynatine® HNS and Placebo
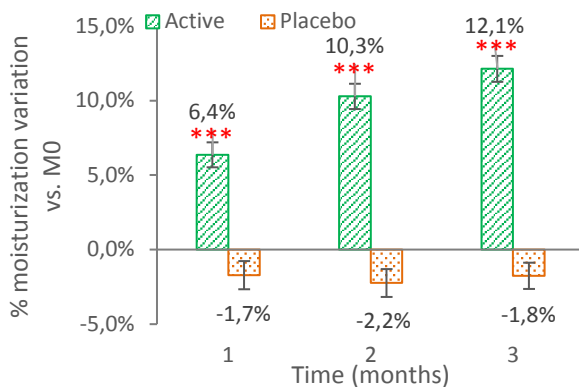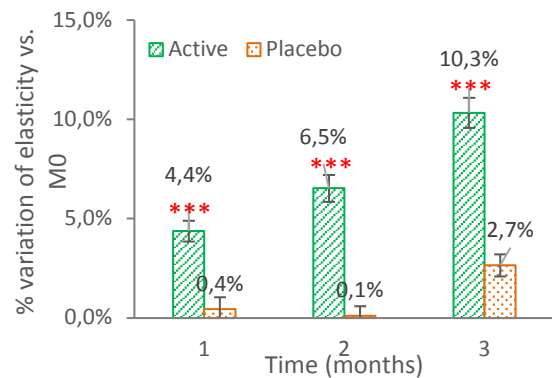
Fig. 13b: mean % of skin elasticity improvement from baseline for Cynatine® HNS and Placebo

Intergroup (Cynatine® HNS vs. Placebo) values determined by t-test, ***$p < 0.001$

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Table 14. Analyses on female and male subjects (Skin– Moisturization and elasticity)

Measured parameters	Female subjects								Male subjects							
	Cynatine® HNS				Placebo				Cynatine® HNS				Pacebo			
	M0	M1	M2	M3	M0	M1	M2	M3	M0	M1	M2	M3	M0	M1	M2	M3
Skin moisturization	38,6% ± 1,1	41,1% ± 1,2	42,6% ± 1,2	43,1% ±1,2	37,7% ± 0,9	36,7% ± 0,9	36,6% ± 0,8	37,0% ± 0,9	42,2% ± 1,9	44,7% ± 1,8	46,1% ± 1,9	47,1% ± 1,9	41,3% ± 1,7	40,7% ± 1,6	40,3% ± 1,5	40,2% ± 1,4
Change to baseline %	-	+6,2%	+10,5%	+11,9%	-	-2,4%	-2,5%	-1,5%	-	+6,5%	+10,0%	+12,4%	-	-1,0%	-2,0%	-2,0%
p-value vs. Baseline	-	p<0,001	p<0,001	p<0,001	-	n.s	n.s	n.s	-	p<0,001	p<0,001	p<0,001	-	n.s.	n.s	n.s
Skin elasticity	0,7238 ±0,0093	0,7565 ± 0,0101	0,7712 ± 0,0098	0,8021 ± 0,0091	0,7351 ±0,0189	0,7354 ±0,0166	0,7311 ±0,0185	0,7552 ±0,0191	0,6981 ±0,0146	0,7265 ±0,0140	0,7415 ±0,0141	0,7640 ± 0,0142	0,7030 ±0,0159	0,7060 ±0,0155	0,7073 ±0,0166	0,7198 ±0,0165
Change to baseline %	-	+4,5%	+6,6%	+11,0%	-	+0,4%	-0,4%	+2,9%	-	+4,2%	+6,4%	+9,7%	-	+0,5%	+0,6%	+2,4%
p-value vs. Baseline	-	p<0,001.	p<0,001.	p<0,001.	-	n.s	n.s	n.s.	-	p<0,01	p<0,001	p<0,001.	-	n.s	n.s	n.s.

*p < 0.05; **p < 0.01; ***p < 0.001

Fig. 14a: Female subjects mean % of skin moisture improvement from baseline for Cynatine® HNS and Placebo.
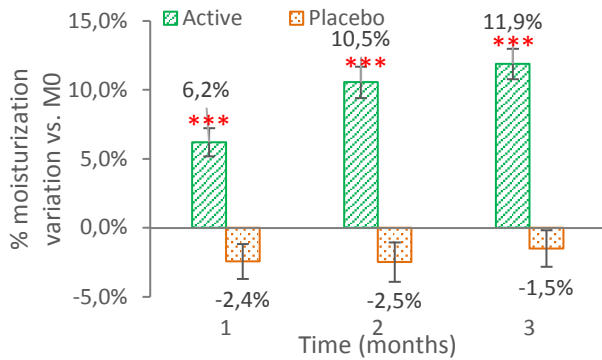
Fig. 14b: Female subjects mean % of skin elasticity improvement from baseline for Cynatine® HNS and Placebo.
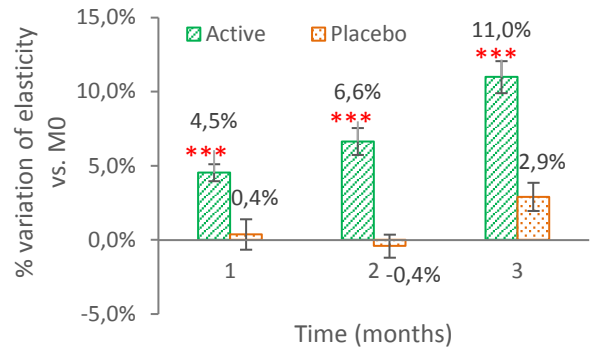

Fig. 14c: Male subjects mean % of skin moisture improvement from baseline for Cynatine® HNS and Placebo
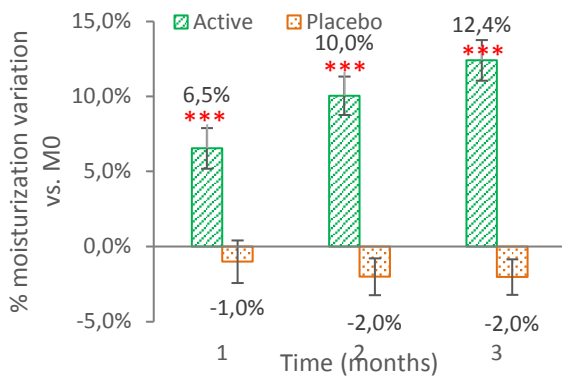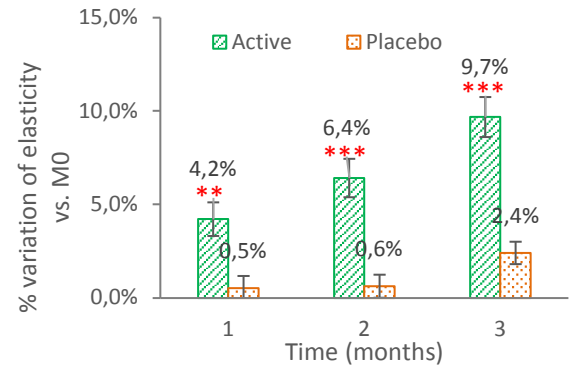
Fig. 14d: Male subjects mean % of skin elasticity improvement from baseline for Cynatine® HNS and Placebo

Intergroup (Cynatine® HNS vs. Placebo) values determined by t-test, **p < 0.01; ***p < 0.001

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Conclusion for overall population and in female and male groups:

- Cynatine® HNS significantly increases the moisture and the elasticity of skin after 30 days up to 12%.
- Cynatine® HNS showed results that were statistically significant to both to baseline and vs. Placebo at 30, 60 and 90 days.
- Cynatine® HNS increases the moisture up to 12% and the elasticity up to 11% after 90 days.

Possible Structure Function Claims:

- Cynatine® HNS supports healthy skin.
- Cynatine® HNS improves the moisture and the elasticity of the skin.
- Cynatine® HNS helps to maintain skin moisture and elasticity.

b. Skin Wrinkles

Skin profilometry is measured using a real 3D microtopography imaging system (Primoslite GFMesstechnik GmbH). Skin surface is reconstructed using an algorithm to generate 3D images. The following skin parameters are measured: maximum wrinkle depth (Sv), surface roughness in vertical direction (Sa), surface roughness in horizontal direction (Sz).

A clinical analysis carried by a board-certified dermatologist is conducted by evaluating the skin wrinkleness at T0 and after 1,2, and 3 months of product use.

Table 15. Analyses wrinkle evaluation on overall population

Measured parameters	Overall subjects							
	Cynatine® HNS				Placebo			
	M0	M1	M2	M3	M0	M1	M2	M3
Skin profilometry **Sa** **(Vertical parameter)**	36,5	35,3	34,1	32,2	37,6	37,4	37,0	38,4
Change to baseline %	-	-3,2%	-6,8%	-12,2%	-	-0,5%	-1,5%	+2,2%
Sz **(Horizontal parameter)**	137,0	133,1	129,9	124,8	134,1	133,0	131,5	135,3
Change to baseline %	-	-3,0%	-5,4%	-9,2%	-	-1,1%	-1,8%	0,8%
Maximum.wrinkle depth **Sv**	454,7	432,8	401,9	391,6	456,9	446,6	460,4	461,1
Change to baseline %	-	-5,1%	-12,2%	-14,4%	-	-2,2%	+1,2%	+1,0%
Clinical evaluation : **Skin wrinkledness** % subjects showing an improvment	-	24,0%	60,0%	68,0%	-	4,0%	12,0%	16,0%

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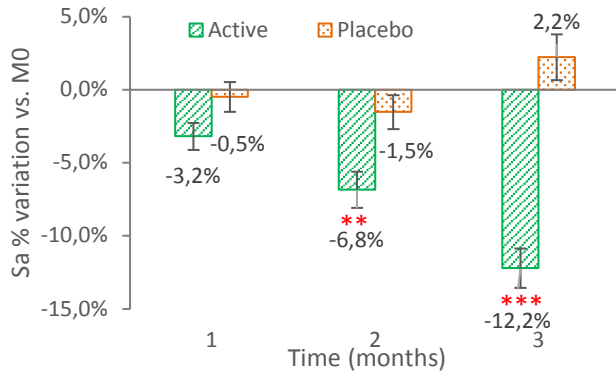Fig. 15a: mean % change in skin roughness (Sa parameter)
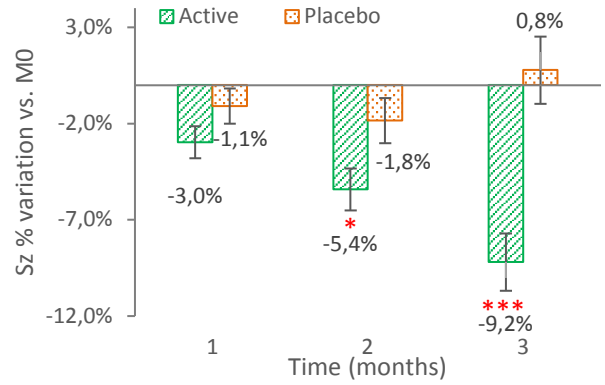
Fig. 15b: mean % change in skin roughness (Sz parameter)

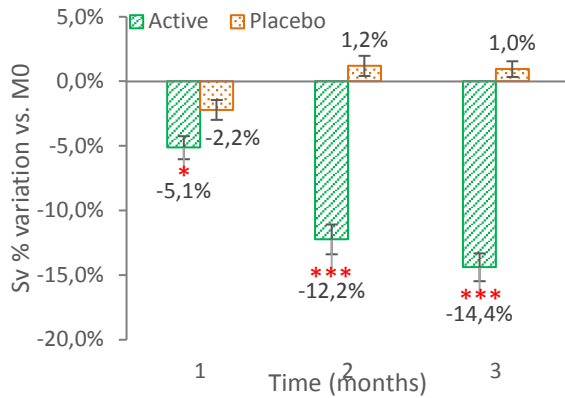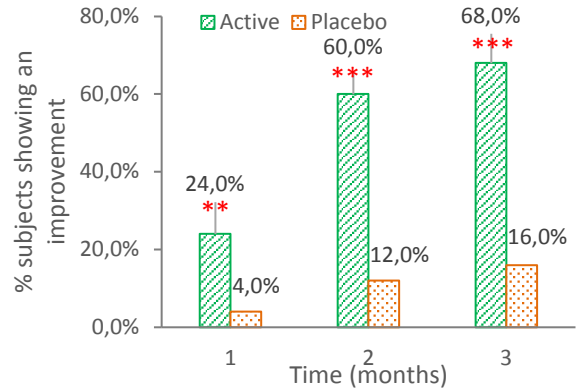Fig. 15c: mean % change in maximum wrinkle depth (Sv parameter)

Fig. 15d: mean % improvement of skin wrinkledness evaluation

Intergroup (Cynatine® HNS vs. Placebo) values determined by t-test, *p < 0.05; **p < 0.01; ***p < 0.001

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37, Av du Mistral Athélia IV
13705 La Ciotat France
Tel: +(0)6 26 18 15 00 Fax +33 04 42 08 89 49 lcarlini@keratinnov.com   Page **18/30**

Table 16. Analyses wrinkle evaluation on female and male subjects

Measured parameters	Female subjects								Male subjects							
	Cynatine® HNS				Placebo				Cynatine® HNS				Pacebo			
	M0	M1	M2	M3	M0	M1	M2	M3	M0	M1	M2	M3	M0	M1	M2	M3
Skin profilometry : Sa (Vertical parameter)	35,2	33,9	33,0	31,6	36,8	36,3	36,4	37,7	37,8	36,7	35,2	32,9	38,4	38,5	37,7	39,2
Change to baseline %	-	-3,3%	-6,6%	-11,2%	-	-0,8%	-1,1%	2,4%	-	-3,1%	-7,1%	-13,3%	-	-0,2%	-2,0%	2,1%
Sz (Horizontal parameter)	141,6	137,2	134,1	127,6	132,4	131,4	130,4	133,9	132,4	129,0	125,6	122,0	135,8	134,6	132,6	136,7
Change to baseline %	-	-3,0%	-5,2%	-9,7%	-	-1,3%	-1,5%	+0,9%	-	-2,9%	-5,6%	-8,6%	-	-0,9%	-2,1%	0,6%
Maximum wrinkle depth Sv	468,7	447,6	416,4	402,6	462,5	450,4	464,3	465,8	440,8	418,0	387,4	380,6	451,2	442,8	456,6	456,4
Change to baseline %	-	-4,8%	-11,9%	-14,8%	-	-2,5%	+1,4%	+0,9%	-	-5,5%	-12,6%	-14,0%	-	-2,0%	+1,0%	+1,0%
Clinical evaluation : Skin wrinkledness % subjects showing an improvement	-	20,0%	56,0%	68,0%	-	4,0%	12,0%	12,0%	-	28,0%	64,0%	68,0%	-	4,0%	12,0%	20,0%

Fig. 16a: mean % change of skin roughness in female subjects (Sa parameter)

Fig. 16b: mean % change of skin roughness in male subjects (Sa parameter)

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13705 La Ciotat France
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Fig. 16c: mean % change of skin roughness in female subjects (Sz parameter)
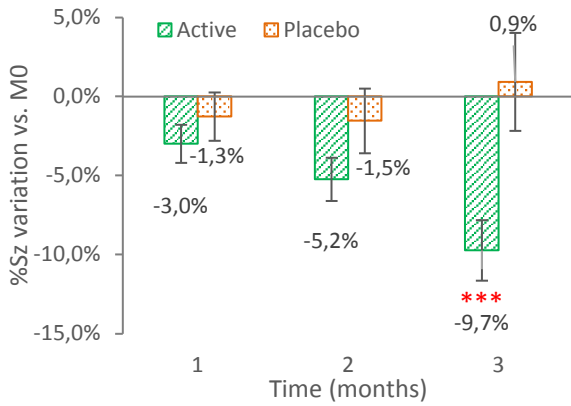

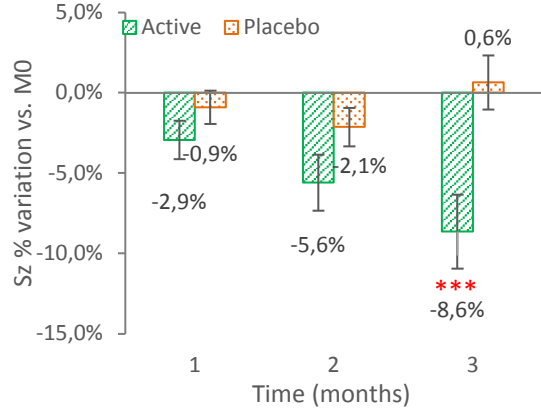Fig. 16d: mean % change of skin roughness in male subjects (Sz parameter)

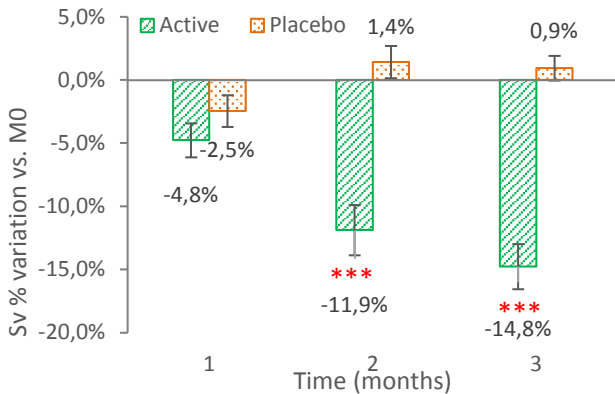Fig. 16e: mean % change of maximum wrinkle depth in female subjects

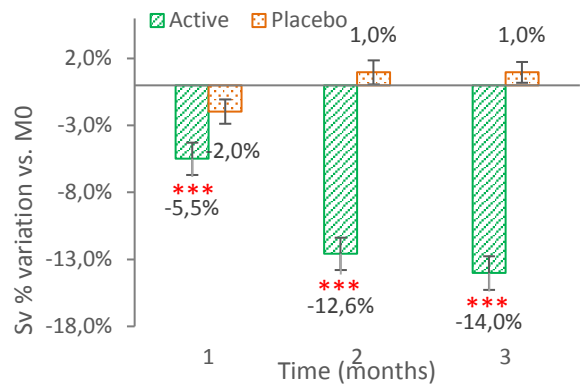Fig. 16f: mean % change of maximum wrinkle depth in male subjects

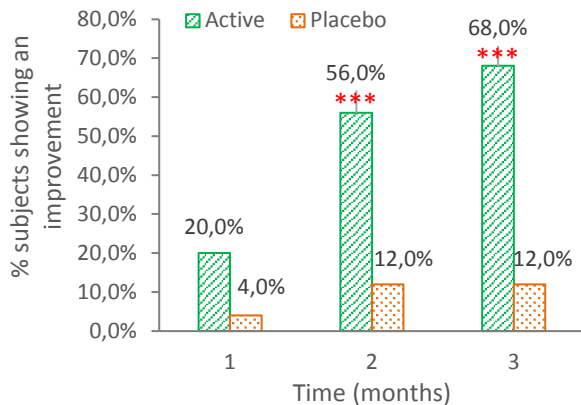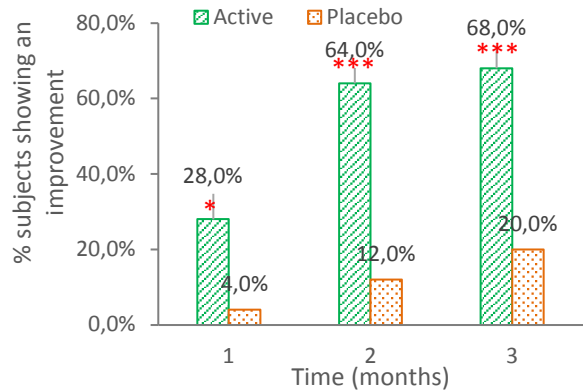Fig. 16g: mean % improvement of skin wrinkledness evaluation in female subjects

Fig. 16h: mean % improvement of skin wrinkledness evaluation in male subjects

Intergroup (Cynatine® HNS vs. Placebo) values determined by t-test, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$

Conclusion for overall population and in female and male groups:

- Cynatine® HNS significantly reduces skin wrinkles after 60 days according to all three measurements.

- Cynatine® HNS 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® HNS had a decrease in skin wrinkles at 60 days, where no more than 55% had the same effect on Placebo.

- Skin smoothness improves in 60% of subjects on Cynatine® HNS 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® HNS decreases skin wrinkles over Placebo by approximately 9 to 18% depending on the measure.

Possible Structure Function Claims:

- Cynatine® HNS supports healthy skin.
- Cynatine® HNS helps reducing skin wrinkles.

c. Skin Cohesion (Protein Content and skin compactness evaluation)

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.

A clinical analysis evaluates the skin compactness by assigning a score according to the following criteria :

Not compact/tonic skin (very low elasticity),

Insufficiently compact/tonic skin (low elasticity,

Compact/tonic, data are reported as % of subjects showing an improvement,

Compact/tonic skin (very elastic skin).

Table 17. Analyses for overall population (Skin–compactness/ Protein Content)

Measured parameters	Overall population							
	Cynatine® HNS				Placebo			
	M0	M1	M2	M3	M0	M1	M2	M3
Protein content (%)	36,9%± 1,1	-	-	27,5% ± 1,1	37,3 ± 1,0	-	-	37,6% ± 1,0
<u>Change to baseline %</u>	-	-	-	-24,3%	-	-	-	+1,2%
Skin compactness (% of improvement)	-	30,0%	42%	58%	-	6%	10%	12%

p < 0.05 is significant.

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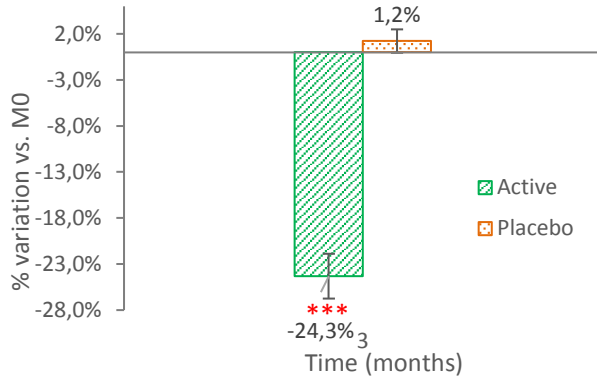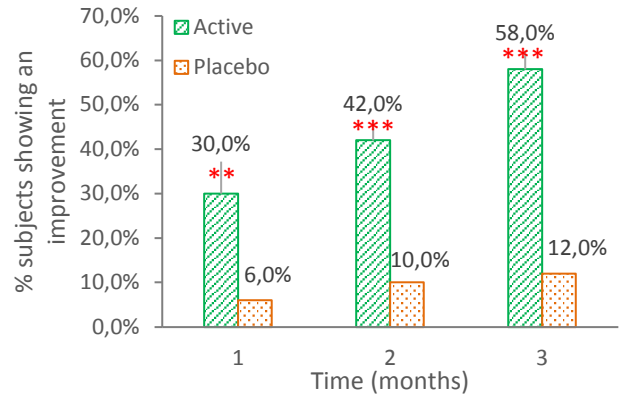Fig. 17a: Mean % change in protein content

Fig. 17b: Mean % improvement of skin compactness evaluation

Intergroup (Cynatine® HNS vs. Placebo) values determined by t-test, *p < 0.05; **p < 0.01; ***p < 0.001

Table 18. Analyses for female and male subjects (Skin– compactness/ Protein Content)

Measured parameters	Female subjects								Male subjects							
	Cynatine® HNS				Placebo				Cynatine® HNS				Pacebo			
	M0	M1	M2	M3	M0	M1	M2	M3	M0	M1	M2	M3	M0	M1	M2	M3
Protein content (%)	40,2% ± 1,6	-	-	27,9% ± 1,9	40,3% ± 1,4	-	-	40,3% ± 1,3	33,5% ± 1,4	-	-	27,0% ± 1,2	34,3 ± 1,7	-	-	34,8% ± 1,3
Change to baseline %	-	-	-	-30,1%	-	-	-	+0,7%	-	-	-	-18,6%	-	-	-	+1,7%
Skin compactness (% improvement)	-	32%	40%	56%	-	8%	8%	8%	-	28%	44%	60%	-	4%	12%	16%

Fig. 18a: Female subjects mean % change in protein content

Fig. 18b: Male subjects mean % change in protein content

Intergroup (Cynatine® HNS vs. Placebo) values determined by t-test, *p < 0.05; **p < 0.01; ***p < 0.001

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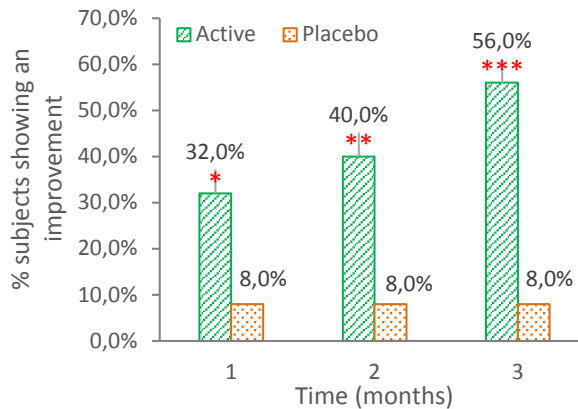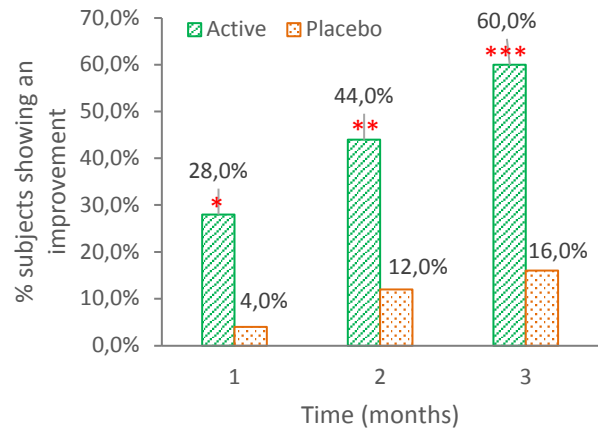Fig. 18c: Female subjects mean % improvement of skin compactness evaluation

Fig. 18d: Male subjects mean % improvement of skin compactness evaluation

Intergroup (Cynatine® HNS vs. Placebo) values determined by t-test, *p < 0.05; **p < 0.01; ***p < 0.001

Conclusion for overall population and in female and male groups:

- Cynatine® HNS improves the compactness and structure of skin after 90 days.
- Cynatine® HNS showed results that were statistically significant versus baseline and versus Placebo at day 90.
- Cynatine® HNS is bioactive based on its ability to improve the protein structure of skin, namely the keratinocytes below the epidermis.
- Products effects on the mesured parameters were comparable between male and female subjects except for the protein content. This difference can be partially explained by a different basal desquamation rate between male and female subjects.

Structure Function Claims:

- Cynatine® HNS supports healthy skin.
- Cynatine® HNS improves the structure and cohesiveness of skin.
- Cynatine® HNS is bioactive.

General conclusion on skin study:

This clinical study demonstrates that Cynatine® HNS (500 mg/day) was effective in improving skin conditions at all experimental monitored checkpoints. The variation obtained in the active group are statically significant from the variation of the Placebo group.

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37, Av du Mistral Athélia IV
13705 La Ciotat France
Tel: +(0)6 26 18 15 00 Fax +33 04 42 08 89 49 lcarlini@keratinnov.com   Page **23/30**

3. EVALUATION OF CYNATINE® HNS ON NAILS

This analysis focuses on multiple mesurements on nail health.

a. Product effect on nails

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 19. Analyses for overall population (Nails status)

Tendency to brake	Overall population	
	Cynatine® HNS	Placebo
	Value ± SD	Value ± SD
Change to baseline :		
Day 30	72%	10%
Day 60	80%	14%
Day 90	94%	26%

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

Fig. 19: Change in nails tendency to break

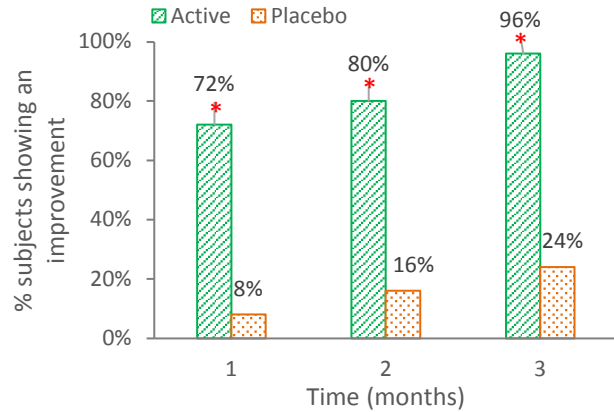Intergroup (Cynatine® HNS vs. Placebo) : **p < 0.01; ***p < 0.001

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Table 20. Analyses for male and female subjects (Nails status)

Tendency to brake	Female subjects		Male subjects	
	Cynatine® HNS	Placebo	Cynatine® HNS	Placebo
	Value ± SD	Value ± SD	Value ± SD	Value ± SD
Change to baseline :				
Day 30	72%	8%	72%	12%
Day 60	80%	16%	80%	12%
Day 90	96%	24%	92%	28%

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

Figure 20a: Female subjects change in nails tendency to break

Figure 20b: Male subjects change in nails tendency to break

*p <0.05 is significant.

Conclusion for overall population and in female and male groups:
- Cynatine® HNS decreases the nails tendency to break even after 30 days and for over 90% of the subjects tested at 90 days.
- Cynatine® HNS showed results that were statistically significant vs. Placebo at 30, 60 and 90 days.
- Cynatine® HNS decreases nails tendency to break by more than 3x Placebo.

Structure Function Claims:
- Cynatine® HNS supports healthy nails.
- Cynatine® HNS reduces nails tendency to break.

b. Nail evaluation

Parameters measurement is carried out by a board-certified dermatologist. Nails status is determinate by according the clinical score scales reported bellow:

Fig. a) Hard nails.

Fig. b) Resistant nails.

Fig. c) Not broken nails; data are reported as % of subjects showing an improvement.

Fig. d) Smooth nails.

Fig. e) White (natural colour) nails.

For all figures, data are reported as % of subjects showing an improvement.

Table 21. Overall population analyses (Nails various parameters)

Measured parameters			Overall population					
			Cynatine® HNS			Placebo		
Subjects at M0	Active	Placebo	M1	M2	M3	M1	M2	M3
Hard nails	30%	28%	40%	52%	60%	8%	10%	14%
Resistant nails	28%	32%	44%	54%	64%	10%	12%	20%
Not brocken nails	48%	52%	24%	34%	42%	0%	8%	10%
Smooth nails	56%	54%	14%	34%	42%	2%	6%	8%
White (natural colour) nails	72%	70%	8%	22%	24%	2%	6%	6%

Fig. 21a: Hard nails

Fig. 21b: Resistant nails

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Fig. 21c: Not broken nails

Fig. 21d: Smooth nails;

Fig. 21e. White (natural color) nails

Table 22. Analyses female and male subjects (Nails various parameters)

Measured parameters			Female subjects						Male subjects					
			Cynatine® HNS			Placebo			Cynatine® HNS			Placebo		
Subjects at M0	Active	Placebo	M1	M2	M3	M1	M2	M3	M1	M2	M3	M1	M2	M3
Hard nails	30%	28%	40%	52%	60%	8%	10%	14%	36%	48%	56%	8%	12%	20%
Resistant nails	28%	32%	44%	54%	64%	10%	12%	20%	36%	48%	56%	8%	8%	16%
Not brocken nails	48%	52%	24%	34%	42%	0%	8%	10%	24%	32%	40%	0%	8%	8%
Smooth nails	56%	54%	14%	34%	42%	2%	6%	8%	16%	36%	40%	4%	8%	12%
White (natural colour) nails	72%	70%	8%	22%	24%	2%	6%	6%	8%	24%	28%	0%	4%	4%

Fig. 22a: Female subjects hard nails   Fig. 22b: Male subjects hard nails

Fig. 22c: Female subjects resistant nails

Fig. 22d: Male subjects resistant nails

Fig. 22e: Female subjects not broken nails
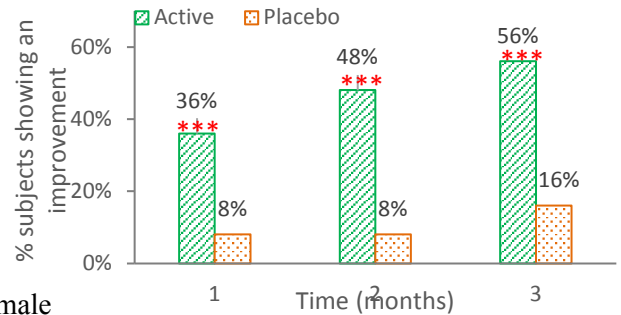

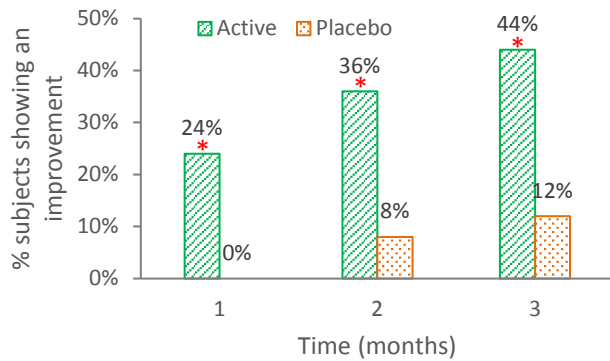Fig. 22f: Male subjects not broken nails
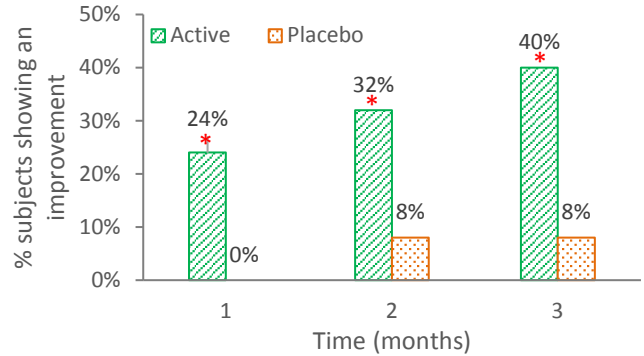

Fig. 22g: Female subjects smooth nails
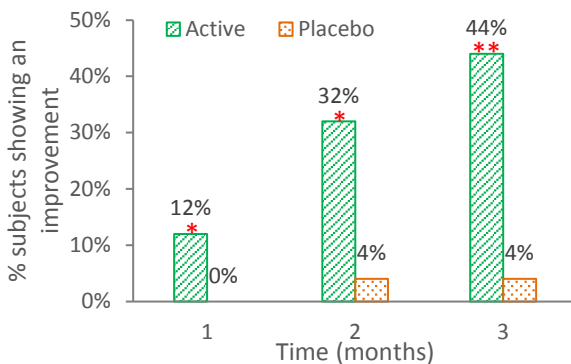

Fig. 22h: Male subjects smooth nails
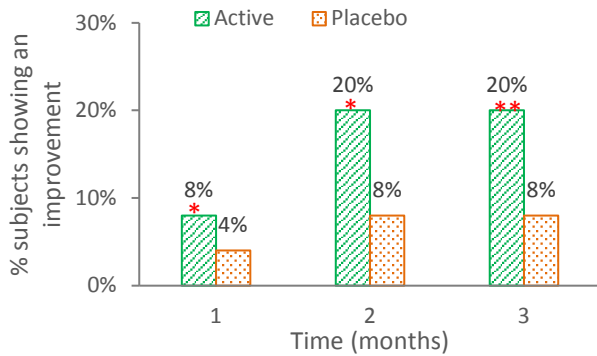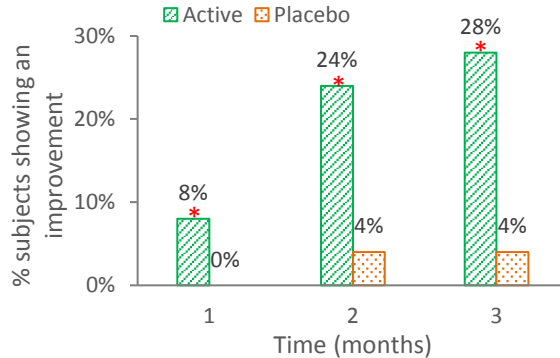
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Fig. 22i: Female subjects white nails

Fig. 22j: Male subjects white nails

General conclusion on nails study:

This clinical study demonstrates the effect of Cynatine® HNS (500mg) in improving the nail conditions.

The product was effective at all the experimental monitored checkpoints.

Product effects on the measured parameters were comparable between male and female subjects.

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 Cynatine® HNS 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:	100 male and female subjects (n=50 Cynatine® HNS group, n=50 Placebo group)
Randomization:	Randomized, double blinded Placebo control study
Study time:	From March 2019 to November 2019
Location:	Complife group, Italy

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Technical Summary of Cynatine® HNS Clinical Trial 2019/0892

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