

# **APPLICATION OF VERSION PEPTIDE FACE CREAM AND VERSION PEPTIDE EYE CREAM ON VOLUNTEERS**

## **CLINICAL STUDY**

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#### **Introduction**

The combination of four oligopeptides (palmitoyl oligopeptide-20, copper peptide-1, palmitoyl pentapeptide-4 and acetyl hexapeptide-8) and dimethylaminoethanol on liposomes of moisturizing agents (hyaluronic acid, betaine) and nutrients (olive squalane, shea butter, vegetable oils, phospholipids) contributes towards delaying aging and improving the appearance of wrinkles.

In this study, VERSION PEPTIDE FACE & EYE creams were applied locally on the face and the area around the eyes on two groups of volunteers. Wrinkle reduction, elasticity increase, skin radiance and skin smoothness were observed. As part of the study, the volunteers filled out self-evaluation forms, while both the volunteers and dermatologists graded the aforementioned properties.

#### **Description**

Aging is manifested on the skin through the formation of wrinkles. This occurs over time and is due to biochemical, histological and physiological changes. Solar radiation plays a pivotal role in aging, contributing to the formation of wrinkles, furrows and lines. Other secondary factors contributing to the formation of wrinkles and furrows include gravity, frequent and constant pressure to the skin during sleep, and muscle contraction from facial expressions.

The molecular changes affect the collagen triple helix, degrade the elastin and, eventually weaken the lipid matrix of the skin. Muscles are contracted when they receive neurotransmitters released from inside a vesicle. The SNARE (SNAP REceptor) complex is essential for this neurotransmitter release at the synapsis (*A. Ferrer Montiel et al, The Journal of Biological Chemistry, 1997, 272, 2634-2638*). The complex is formed by the VAMP, Syntaxin and SNAP-25 (SyNaptosomal Associated Protein) proteins. This complex acts like a cellular hook, which captures the vesicles and fuses them to the cell membranes for the release of neurotransmitters.

Acetyl hexapeptide-8 comes from the biochemical pathway to GMP production. It was the study of the basic biochemical mechanisms of anti-wrinkle activity that led to the discovery of this hexapeptide. It may also be considered a substitute to Botulinum Toxin A, which carries a very high cost. It acts on the facial muscles in a different manner. The Acetyl hexapeptide-8 molecule is a mimic of the N-terminal end of SNAP-25, which competes with SNAP-25 for a position in the SNARE complex, thereby modulating its formation. If the SNARE complex is slightly destabilized, the vesicle cannot release neurotransmitters efficiently and, therefore, muscle contraction is attenuated, preventing the formation of lines and wrinkles. This way, Acetyl hexapeptide-8 reduces the depth of wrinkles on the forehead and around the eyes caused by the contraction of muscles due to facial expressions. It is a safer and cheaper alternative to Botulinum Toxin. It acts topically and prevents the wrinkle-formation mechanism in a very different way to Botulinum Toxin.

Copper tripeptide-1 activates the production of proteoglycans and glycosaminoglycans, which are essential structural elements of the skin. Along with Oligopeptide-20, they improve skin elasticity and soften wrinkles, while boosting collagen and elastin synthesis. Palmitoyl Pentapeptide-4 and dimethylaminoethanol contribute to the reduction of wrinkles and fine lines in photo-aged face skin.

All these are trapped in liposomes, spherical vesicles formed by phospholipid bilayers that protect the encapsulated substances from chemical and enzymatic reactions, and ensure penetration of active ingredients, slow release and long-term efficacy.

The action of oligopeptides is supported by moisturizing agents (hyaluronic acid, betaine) and nutrients (olive squalane, shea butter, vegetable oils, phospholipids), which contribute towards moisturizing and enhancing the skin barrier.

### **Study design and materials**

VERSION PEPTIDE FACE CREAM and VERSION PEPTIDE EYE CREAM were used topically for the purposes of this study. A total of **23 patients** participated, who graded the aesthetic result with regard to wrinkle reduction, radiance, elasticity and smoothness. The self-evaluation was performed on the 1<sup>st</sup>, 5<sup>th</sup>, 9<sup>th</sup> and 12<sup>th</sup> week. The dermatologists also performed a similar grading on the same dates. No adverse effects were recorded for any of the products during the study.

## Results

The first table pertains to **wrinkle reduction**. The volunteers were asked to observe the nasolabial furrows and grade the thickness reduction.

### 1. WRINKLE REDUCTION

#### 1.1 SELF-EVALUATION

Scale 0-3

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	0	1	1	2
2	1	1	2	2
3	0	1	2	2
4	0	1	2	2
5	1	2	3	3
6	0	1	2	3
7	1	1	2	3
8	0	1	1	2
9	0	1	2	2
10	0	1	2	2
11	1	1	3	3
12	1	1	2	3
13	0	1	1	2
14	0	2	2	3
15	1	1	2	2
16	1	2	2	3
17	1	2	2	3
18	1	2	2	2
19	0	1	1	2
20	0	0	2	2

21	1	1	2	3
22	1	1	2	2
23	0	1	2	2
Mean score**	0.4783	1.1739	1.9130	2.3913
Percentage***		65% Week 5--- Week 1	74% Week 9--- Week 5	48% Week 12--- Week 9
Percentage***			100% Week 9--- Week 1	100% Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

$$\frac{\text{Total score}}{\text{Number of volunteers}}$$

$$\frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$$

Wilcoxon test  
 Week 1–Week 5 p<0.05  
 Week 1–Week 9 p<0.05  
 Week 1–Week 12 p<0.05  
 Week 5–Week 9 p<0.05  
 Week 5–Week 12 p<0.05  
 Week 9–Week 12 p<0.05

**1. WRINKLE REDUCTION**  
**1.2 EVALUATION BY DERMATOLOGIST**

Scale 0-5

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	0	2	2	3
2	1	1	3	3
3	1	2	2	3
4	0	1	2	3

5	1	2	3	3
6	1	3	3	4
7	1	2	2	4
8	1	2	2	3
9	0	1	2	3
10	0	1	2	3
11	1	2	4	4
12	0	2	3	3
13	0	1	1	3
14	0	2	3	4
15	1	2	2	3
16	1	3	3	4
17	1	2	3	4
18	1	2	2	3
19	0	1	2	3
20	0	1	2	3
21	1	1	3	3
22	1	2	3	4
23	0	2	3	3
Mean score*	0.5652	1.7391	2.4783	3.3043
Percentage**		91% Week 5--- Week 1	61% Week 9--- Week 5	74% Week 12--- Week 9
Percentage***			100% Week 9--- Week 1	100% Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

$$\frac{\text{Total score}}{\text{Number of volunteers}}$$
\*\*

$$\frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$$
\*\*\*

Wilcoxon test

Week 1–Week 5  $p < 0.05$

Week 1–Week 9  $p < 0.05$

Week 1–Week 12  $p < 0.05$

Week 5–Week 9  $p < 0.05$

Week 5–Week 12  $p < 0.05$

Week 9–Week 12  $p < 0.05$

## **CONCLUSION ON WRINKLE REDUCTION:**

### **SELF-EVALUATION**

65% of volunteers showed a statistically significant improvement from Week 1 to Week 5. 74% of patients showed statistically significant improvement from Week 5 to Week 9, while 48% from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, wrinkles decreased by half in Week 5 compared with Week 1, and by three-quarters in Week 9 compared with Week 1; they decreased to one-fifth in Week 12 compared with Week 1.

### **EVALUATION BY DERMATOLOGIST**

91% of volunteers showed a statistically significant improvement from Week 1 to Week 5. 61% of patients showed some improvement from Week 5 to Week 9, while 74% from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, wrinkles decreased by two-thirds in Week 5 compared with Week 1, and by three-quarters in Week 9 compared with Week 1; they decreased to one-sixth in Week 12 compared with Week 1.

## 2. ELASTICITY INCREASE

### 2.1 SELF-EVALUATION

Scale 0-3

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	1	1	2	2
2	1	2	2	2
3	1	1	2	3
4	0	1	1	2
5	1	2	2	3
6	0	1	1	3
7	0	2	2	3
8	0	1	2	2
9	0	2	2	3
10	1	2	2	2
11	1	2	2	3
12	1	1	2	2
13	0	1	2	2
14	0	2	2	2
15	1	1	2	2
16	1	2	2	3
17	1	2	2	3
18	0	1	2	2
19	1	1	2	2
20	0	1	2	2
21	0	2	2	3
22	1	1	2	2
23	0	1	1	3

Mean score*	0.5217	1.4348	1.8696	2.4348
Percentage**		78% Week 5--- Week 1	43% Week 9--- Week 5	48% Week 12--- Week 9
Percentage***			100 Week 9--- Week 1	100 Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

Total score

\*\* Number of volunteers

\*\*\*  $\frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$

Wilcoxon test

Week 1–Week 5 p<0.05

Week 1–Week 9 p<0.05

Week 1–Week 12 p<0.05

Week 5–Week 9 p<0.05

Week 5–Week 12 p<0.05

Week 9–Week 12 p<0.05

## 2. ELASTICITY INCREASE

### 2.2 EVALUATION BY DERMATOLOGIST

Scale 0-5

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	1	2	2	3
2	1	2	2	3
3	1	2	3	4
4	0	2	3	3
5	1	2	3	3
6	1	2	2	3
7	0	2	3	4



8	0	1	2	3
9	0	1	1	3
10	1	2	3	3
11	1	2	3	4
12	0	2	2	3
13	0	1	2	3
14	0	2	3	4
15	1	2	2	3
16	1	3	3	4
17	1	1	3	3
18	0	1	2	3
19	0	1	2	3
20	1	1	3	3
21	1	2	2	3
22	1	2	3	4
23	1	2	2	3
Mean score**	0.6087	1.7391	2.4348	3.2609
Percentage***		96% Week 5--- Week 1	57% Week 9--- Week 5	78% Week 12--- Week 9
Percentage***			100% Week 9--- Week 1	100% Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

$$\frac{\text{Total score}}{\text{Number of volunteers}}$$
  
 \*\*

$$*** \frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$$

Wilcoxon test

Week 1–Week 5  $p < 0.05$

Week 1–Week 9  $p < 0.05$

Week 1–Week 12  $p < 0.05$

Week 5–Week 9  $p < 0.05$

Week 5–Week 12  $p < 0.05$

Week 9–Week 12  $p < 0.05$

## **CONCLUSION ON ELASTICITY:**

### **SELF-EVALUATION**

78% of volunteers showed a statistically significant improvement from Week 1 to Week 5. 43% of patients showed statistically significant improvement from Week 5 to Week 9, while 48% from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, elasticity almost tripled in Week 5 compared with Week 1 and quadrupled in Week 9 compared with Week 1; it was five times greater in Week 12 compared with Week 1.

### **EVALUATION BY DERMATOLOGIST**

96% of volunteers showed a statistically significant improvement from Week 1 to Week 5. In statistical terms, 57% of patients showed a significant improvement from Week 5 to Week 9, while 78% showed such an improvement from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, elasticity almost tripled in Week 5 compared with Week 1 and quadrupled in Week 9 compared with Week 1; it was five times greater in Week 12 compared with Week 1.

**3. SKIN RADIANCE**  
**3.1 SELF-EVALUATION**

SCALE 0-3

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	0	1	2	2
2	1	2	2	3
3	0	1	2	2
4	0	1	1	2
5	1	2	3	3
6	1	2	3	3
7	0	1	1	3
8	1	1	2	2
9	0	1	2	3
10	0	1	1	2
11	1	2	3	3
12	1	2	2	3
13	0	1	2	2
14	1	2	3	3
15	1	1	2	2
16	1	2	2	3
17	1	2	2	3
18	1	1	2	2
19	0	1	2	2
20	0	1	2	2
21	1	2	3	3
22	1	2	2	2
23	1	1	2	2

Mean score**	0.6087	1.4348	2.0870	2.4783
Percentage***		87% Week 5--- Week 1	65% Week 9--- Week 5	35% Week 12--- Week 9
			100% Week 9--- Week 1	100% Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

\*\*  $\frac{\text{Total score}}{\text{Number of volunteers}}$

\*\*\*  $\frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$

Wilcoxon test

Week 1–Week 5 p<0.05

Week 1–Week 9 p<0.05

Week 1–Week 12 p<0.05

Week 5–Week 9 p<0.05

Week 5–Week 12 p<0.05

Week 9–Week 12 p<0.05

### 3. SKIN RADIANCE

#### 3.2 EVALUATION BY DERMATOLOGIST

SCALE 0-5

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	0	2	3	4
2	1	2	3	4
3	0	2	3	3
4	0	2	2	3
5	1	2	3	4
6	1	3	4	5
7	1	2	3	5

8	1	2	3	3
9	0	1	2	3
10	0	2	2	3
11	1	2	4	5
12	1	2	2	4
13	0	1	2	3
14	1	2	3	4
15	1	2	2	3
16	1	3	3	5
17	1	2	3	4
18	1	2	3	3
19	0	1	3	4
20	0	2	2	3
21	1	2	3	4
22	1	2	2	5
23	1	2	3	3
Mean score**	0.6522	1.9565	2.7391	3.7826
Percentage***		100% Week 5--- Week 1	70% Week 9--- Week 5	83% Week 12--- Week 9
Percentage***			100% Week 9--- Week 1	100% Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

$$\frac{\text{Total score}}{\text{Number of volunteers}}$$
  
\*\*

$$*** \frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$$

Wilcoxon test

Week 1–Week 5  $p < 0.05$

Week 1–Week 9  $p < 0.05$

Week 1–Week 12  $p < 0.05$

Week 5–Week 9  $p < 0.05$

Week 5–Week 12  $p < 0.05$

Week 9–Week 12  $p < 0.05$

## **CONCLUSION ON RADIANCE:**

### **SELF-EVALUATION**

87% of volunteers showed a statistically significant improvement from Week 1 to Week 5. 65% of patients showed some improvement from Week 5 to Week 9, while 35% from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, radiance almost doubled in Week 5 compared with Week 1 and tripled in Week 9 compared with Week 1; it was four times greater in Week 12 compared with Week 1.

### **EVALUATION BY DERMATOLOGIST**

All volunteers showed a statistically significant improvement from Week 1 to Week 5. 70% of patients showed some improvement from Week 5 to Week 9, while 83% from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, radiance almost tripled in Week 5 compared with Week 1, and quadrupled in Week 9 compared with Week 1; it was six times greater in Week 12 compared with Week 1.

#### 4. SKIN SMOOTHNESS

##### 4.1 SELF-EVALUATION

SCALE 0-3

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	0	1	1	2
2	0	1	2	2
3	0	1	1	2
4	0	1	2	2
5	1	1	2	2
6	0	2	2	3
7	1	2	2	3
8	0	1	1	2
9	1	1	2	3
10	0	2	2	3
11	0	1	2	3
12	1	2	2	2
13	1	2	2	3
14	0	2	2	2
15	1	1	2	3
16	1	1	2	3
17	0	2	2	3
18	0	2	2	2
19	1	2	2	2
20	1	1	2	3
21	1	2	3	3
22	1	2	2	2
23	0	1	2	2

Mean score**	0.4783	1.4783	1.9130	2.4783
Percentage***		78% Week 5--- Week 1	48% Week 9--- Week 5	57% Week 12--- Week 9
Percentage***			100% Week 9--- Week 1	100% Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

\*\*  $\frac{\text{Total score}}{\text{Number of volunteers}}$

\*\*\*  $\frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$

Wilcoxon test  
 Week 1–Week 5 p<0.05  
 Week 1–Week 9 p<0.05  
 Week 1–Week 12 p<0.05  
 Week 5–Week 9 p<0.05  
 Week 5–Week 12 p<0.05  
 Week 9–Week 12 p<0.05

**4. SKIN SMOOTHNESS**  
**4.2 EVALUATION BY DERMATOLOGIST**

SCALE 0-5

Volunteers	Week 1*	Week 5	Week 9	Week 12
1	0	1	2	3
2	0	2	3	3
3	0	2	3	3
4	0	1	2	2
5	0	2	3	3
6	1	1	2	3
7	1	2	3	4



8	0	1	1	3
9	0	1	2	4
10	1	3	3	4
11	1	1	2	3
12	1	2	2	3
13	0	2	2	3
14	0	2	3	4
15	1	2	2	4
16	1	2	3	3
17	0	2	3	4
18	0	1	2	3
19	1	2	2	3
20	1	2	3	4
21	1	1	2	3
22	1	2	2	3
23	1	1	3	4
Mean score**	0.5217	1.6522	2.3913	3.3043
Percentage***		83% Week 5--- Week 1	70% Week 9--- Week 5	78% Week 12--- Week 9
Percentage***			100% Week 9--- Week 1	100% Week 12--- Week 1

\*Neither the cosmetic product under study nor any other cosmetic products were used in Week 1.

$$\frac{\text{Total score}}{\text{Number of volunteers}}$$
  
\*\*

$$*** \frac{\text{Number of volunteers reported improvement}}{\text{Total number of volunteers}} \times 100$$

Wilcoxon test

Week 1–Week 5  $p < 0.05$

Week 1–Week 9  $p < 0.05$

Week 1–Week 12  $p < 0.05$

Week 5–Week 9  $p < 0.05$

Week 5–Week 12  $p < 0.05$

Week 9–Week 12  $p < 0.05$

## **CONCLUSION ON SKIN SMOOTHNESS:**

### **SELF-EVALUATION**

78% of volunteers showed a statistically significant improvement from Week 1 to Week 5. 48% of patients showed statistically significant improvement from Week 5 to Week 9, while 57% from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, smoothness almost tripled in Week 5 compared with Week 1 and quadrupled in Week 9 compared with Week 1; it was five times greater in Week 12 compared with Week 1.

### **EVALUATION BY DERMATOLOGIST**

83% of volunteers showed a statistically significant improvement from Week 1 to Week 5. In statistical terms, 70% of patients showed a significant improvement from Week 5 to Week 9, while 78% showed such an improvement from Week 9 to Week 12. All volunteers showed some improvement, significant in statistical terms, in Week 9 compared with Week 1, as well as in Week 12 compared with Week 1. On average, smoothness almost tripled in Week 5 compared with Week 1 and quadrupled in Week 9 compared with Week 1; it was six times greater in Week 12 compared with Week 1.

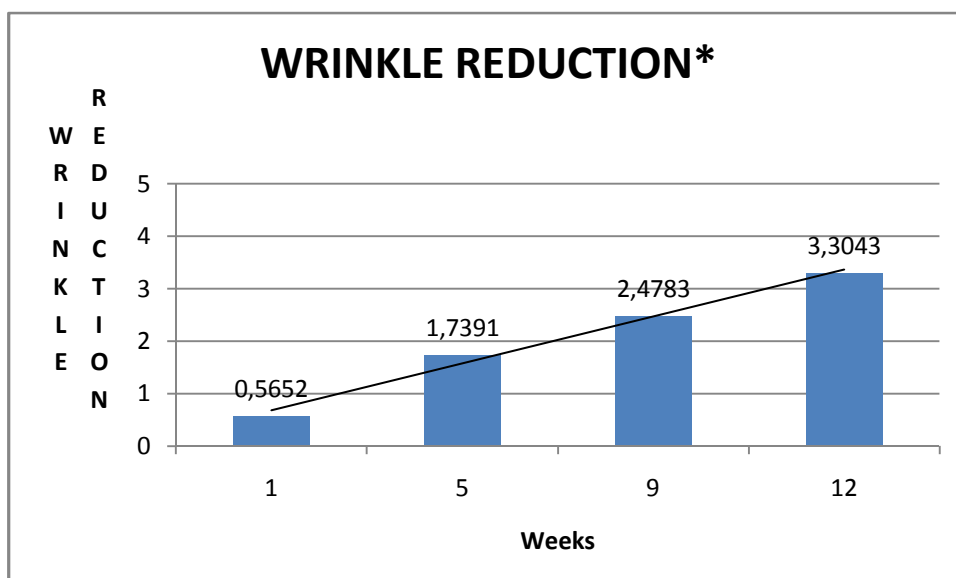
## GRAPHS

### 1.1 Wrinkle reduction according to the self-evaluation (Scale 0-3)



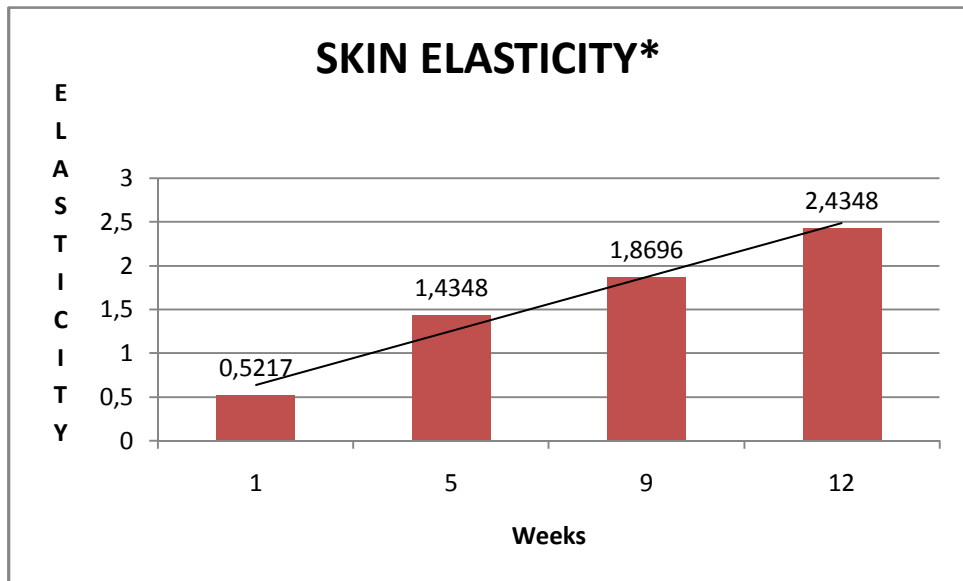
\* $p < 0.05$  statistically significant

### 1.2 Wrinkle reduction according to the dermatologist's evaluation (Scale 0-5)



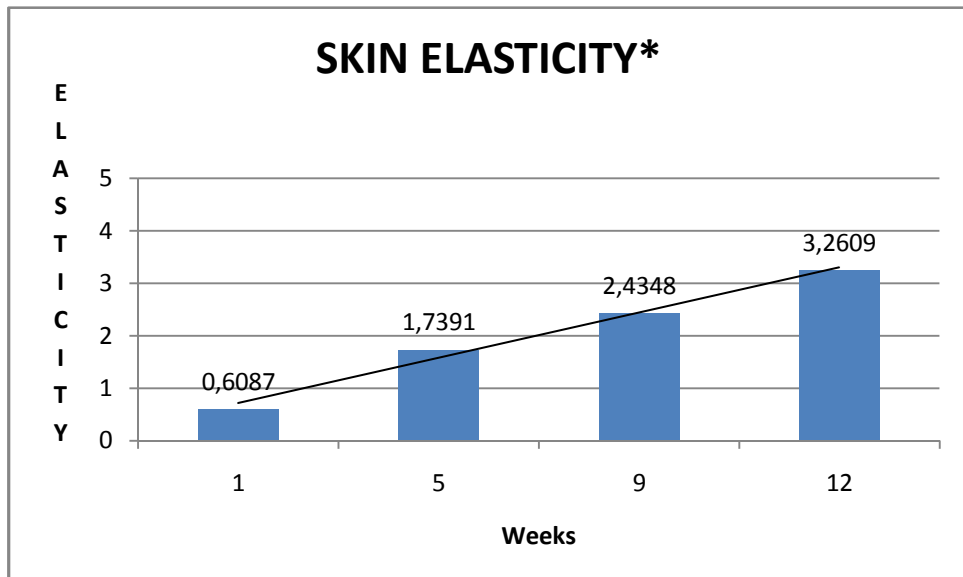
\* $p < 0.05$  statistically significant

2.1 Skin elasticity increase according to the self-evaluation  
(Scale 0-3)



\* $p < 0.05$  statistically significant

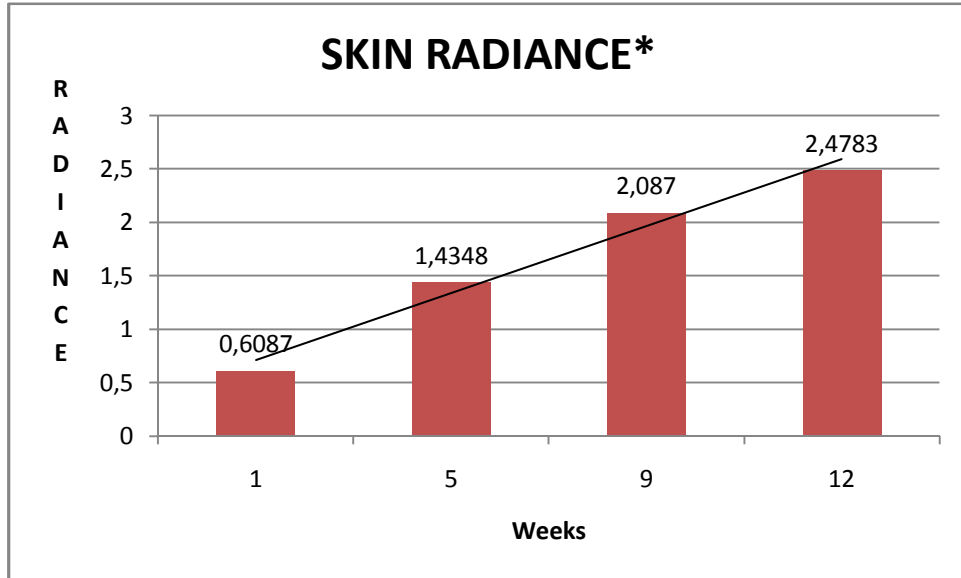
2.2 Skin elasticity increase according to the dermatologist's evaluation  
(Scale 0-5)



\* $p < 0.05$  statistically significant

### 3.1 Skin radiance according to the self-evaluation

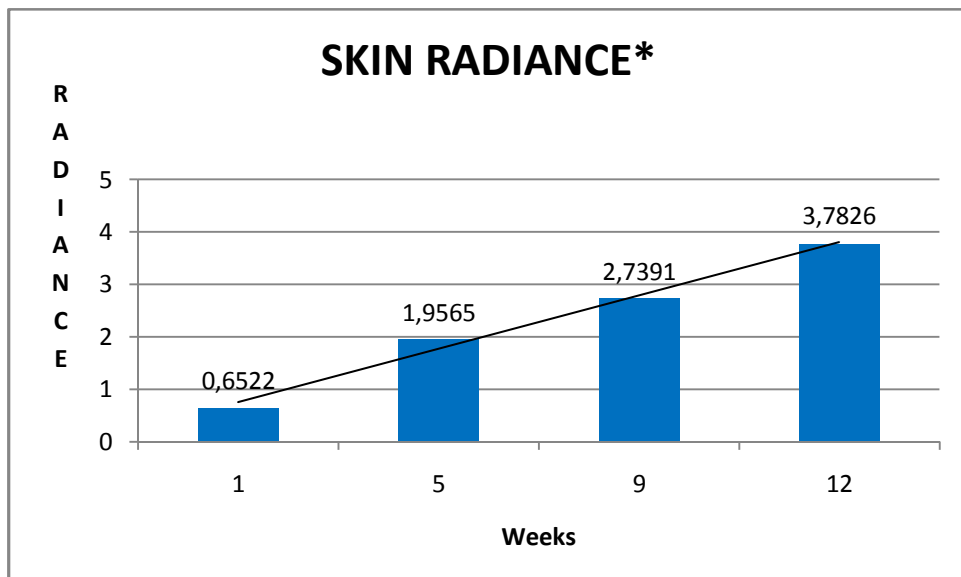
(Scale 0-3)



\*p<0.05 statistically significant

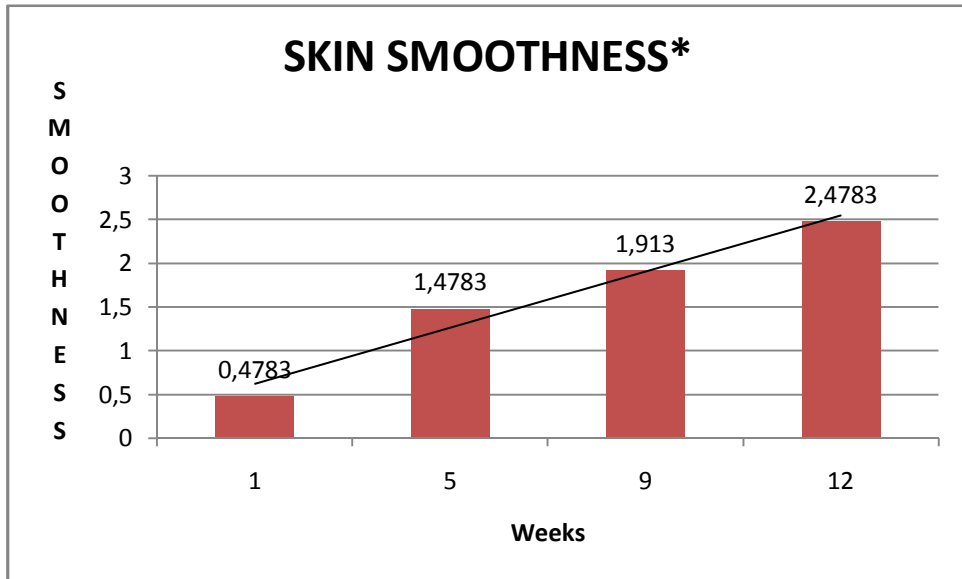
### 3.2 Skin radiance according to the dermatologist's evaluation

(Scale 0-5)



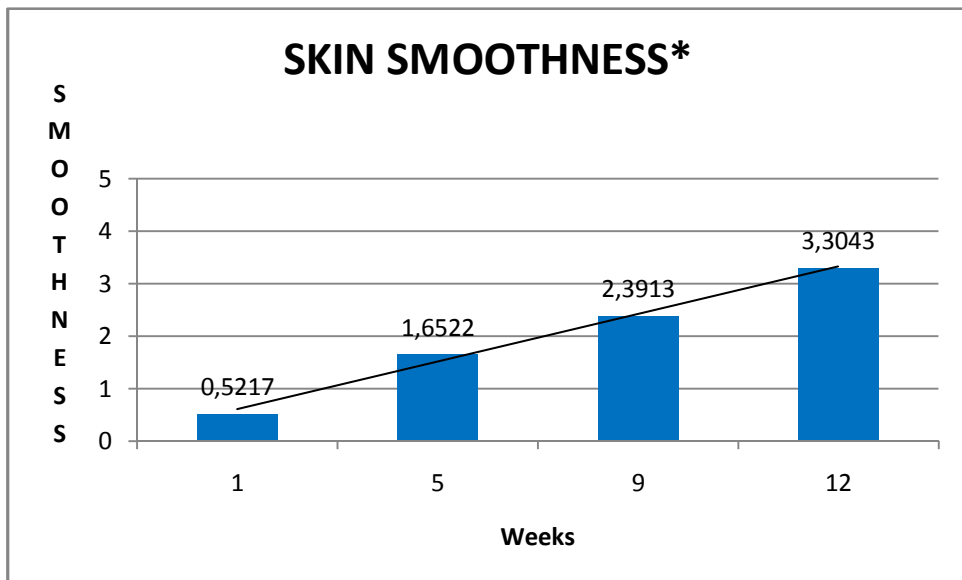
\*p<0.05 statistically significant

4.1 Skin smoothness according to the self-evaluation  
(Scale 0-3)



\*p<0.05 statistically significant

4.2 Skin smoothness according to the dermatologist's evaluation  
(Scale 0-5)



\*p<0.05 statistically significant

## **CONCLUSIONS**

The study of the volunteers' skin after the local application of the VERSION PEPTIDE FACE and EYE CREAM skin cosmetics provided statistical data on reduction of nasolabial furrows, skin elasticity improvement, skin smoothness and radiance increase. The observations were evaluated both by the volunteers and by the dermatologists who participated in the study. The products were deemed safe, since no adverse effects were detected, and effective against aging. They are an alternative anti-aging treatment to Botulinum Toxin A, which is invasive, painful (since it is injected) and costly. Taking into account all the parameters we examined, we believe that the VERSION PEPTIDE FACE and EYE CREAM cosmetic products are safe and can be used to prevent aging.