Biomimetic endorphin for wrinkle lifting in a daily cosmetic remedy.

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Abstract

Background: Over time there has been an evolution in cosmetics to find substances that can minimize the signs of aging. In this scenario, peptides play an essential role in obtaining a lifted skin face. The most effective substance used as a lifting ally is the botulinum toxin; subsequently, to its discovery, several biomimetic peptides were synthesized to find other valid compounds. The developed SH-Pentapeptide-5 is an endorphin peptide associated with a delivery system based on Conjugated Linoleic Acid (CLA) amidified with Glutathione. This innovative system, tested in vivo compared to placebo through a single-blind clinical trial, carried out the following actions when applied topically on the panelists' skin face. Methods: This innovative system, tested in vivo compared to placebo through a single-blind clinical trial, carried out the following actions when applied topically on the panelists' skin face.

1) Soothing action: the CLA is a precursor of the anti-inflammatory PGE2 that gives an anti-aging effect linked to the micro skin inflammations relief.

2) Damaged skin repair: through interaction with the hemidesmosomes. The in vivo tested peptide causes the disassembly of the hemidesmosome chains favoring cell migration towards damaged skin areas to heal tissue wounds.

3) Botox-like effect for endorphin-like action: the peptide acts on the neuromuscular synaptic junction in the facial muscles, where through interaction with its target, delta-opioid receptor, it determines a hyperpolarizing effect on the presynaptic neuron. This hyperpolarization inhibits the acetylcholine release; in this way, muscle excitability is inhibited. As a result, the mimic muscle relaxes, and the expression lines are less visible. Results: results show that the Gluthathione-CLA-SHPentapeptide-5 is a promising ally in treating typical aging dysfunctions. It can lift face wrinkles and firm the skin when applied twice a day topically for a month. In contrast with other peptides like the botulinum toxin, this system is not an injective treatment; consequently, it does not cause side effects, and in addition, it can be conveyed in cosmetic formulations without the need for medical intervention. Conclusion: results show that the Gluthathione-CLA-SHPentapeptide-5 is a promising ally in treating typical aging dysfunctions. It can lift face wrinkles and firm the skin when applied twice a day topically for a month. In contrast with other peptides like the botulinum toxin, this system is not an injective treatment; consequently, it does not cause side effects, and in addition, it can be conveyed in cosmetic formulations without the need for medical intervention.

Keywords: Cosmeceutical, Endorphin, Botox-like, Biomimetic peptide, Cosmetic trial.

Introduction

Nowadays, our skin is much more stressed because everything is swift. Stress alters many essential skin functions through catecholamine booster, oxidation processes, dehydration, and skin barrier alteration [1].

When it happens, cells contract and lose their original order; they can no longer perform their functions properly. All those typical aging processes begin in this disordered state: discoloration, dryness, atony, and irregularity [2]. This continuous demand for prevention, reduction, or mitigation of the signs of aging leads to the development of innovative cosmetic products [3]. Dermatological cosmetics offer topical formulas, "lifting effect," or "botox like" touch-ups without

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scalpels, inspired by aesthetic medicine. This category includes biomimetic peptides (BMP).

Bioactive peptides are small amino acid chains, typically 2-50 aa, derived mainly from the enzymatic digestion of complex proteins, such as collagen, elastin, and fibronectin.

Some occur naturally in the human body and play different biological roles, particularly as signaling/regulating molecules in various physiological processes, including defense, immunity, stress, growth, homeostasis, and reproduction [4,5].

Biomimetic peptides can be synthesized biotechnologically. They mimic the action of inner molecules, like growth factors, neurotransmitters, and cytokines, by interacting with their receptors, bringing clinical effects such as slowing down aging [6].

Thanks to their versatility, other biomimetic peptides have been investigated for their cosmetic use, which has proved to be very useful as anti-aging active ingredients and in skin cell repair [7,8].

Topical BMPs consist of amino acids with modified acid chains, enhancing an existing physiological function and improving pharmacokinetics such as increased permeability, stability, solubility, and better interaction with cellular receptors [9-11].

Examples of BMPs include Oligopeptide-34, which decreases melanin synthesis and tyrosinase activity in skin melanocytes and reduces the transfer of melanosomes to keratinocytes [12]. Oligopeptide-72 inhibits the hyaluronidases, ensuring an even and natural filler absorption over time, leading to a long-lasting result [13]. Acetyl-decapeptide-3 reduces and prevents wrinkles by generating new cells, and it is involved in natural growth, repairing, and the skin-strengthening process by boosting collagen and elastin. The oligopeptide-51 decreases tyrosinase, TRP-1, and TRP-2 expression reducing and preventing the formation of wrinkles by actively regenerating new skin cells [14].

In addition to the mechanisms of action already mentioned, BMPs can inhibit the release of neurotransmitters at the level of neuromuscular junctions: vesicles containing the neurotransmitter acetylcholine (Ach) must be released into the neuromuscular junctions where they interact with SNARE complexes (activating protein of the soluble receptor sensitive N-ethylmaleimide factor). This process is modulated by a receptor protein, SNAP-25, a membrane protein that binds to the vesicle and directly regulates the binding and fusion of vesicles involving the SNARE complex [15].

Some peptides possess structural similarities with the SNAP-25 proteins of SNARE complexes and compete for these binding sites, destabilizing their structure and preventing the release of Ach at nerve endings, modulating the actions of this neurotransmitter [4,16,17]. Peptides of this class are used in anti-aging cosmetics to attenuate the formation of wrinkles as they favor the involuntary movement of facial muscles. These peptides have been shown to inhibit neurosecretion and are called neurotransmitter inhibitor peptides [18].

The endorphin peptide SH-Pentapeptide-5, marketed as Peptilift (Kalichem Srl, 25086 Rezzato, Italy), is a biomimetic endorphin peptide-functionalized with an innovative releasing system that provides the skin with endorphins shock, acting at different levels. Like neurotransmitters, neuropeptides are released by nerve endings and are recognized by specific receptors on target cells.

Endogenous opioids are polypeptides with different dimensions grouped into four families: enkephalins, endorphins, dynorphins, and orphans. Their receptors are all metabotropic, therefore consisting of 7 transmembrane helices coupled to the inhibitory Gi protein, which reduces cAMP through the adenylate cyclase inhibition and activates K^+-channels leading to membrane hyperpolarization [19]. Thus morphine-like peptides, enkephalins, and endorphins act on opioid receptors and are implicated in the modulation of pain sensitivity and skin-repairing mechanisms [20].

Thanks to its endorphins structure, Peptilift acts on the opioid δ-receptor, too. The potential current that generates the pain induces the opening of the VOC sodium channels and, subsequently, the opening of the VOC calcium channels. Since the membrane is hyperpolarized due to the presence of opioids, there is less input of calcium, more diminutive vesicles fusion, and neurotransmitter release, leading to less intense excitatory postsynaptic potential.

The investigated peptide inhibits neuromuscular synapses in mimic muscles, acting with the exact mechanism as leu-enkephalins. Peptilift induces hyperpolarization of the presynaptic neuron on the neuromuscular junction through interaction with the δ-opioid receptor. This hyperpolarization inhibits the Ach release, so the postsynaptic membrane is not depolarized, and muscle excitability is inhibited. As a result, the mimic muscle relaxes, and the expression wrinkle is less visible.

More precisely, Peptilift is not only an endorphin-like peptide; it is a complex containing a delivery system based on Conjugated Linoleic Acid (CLA) amided with Glutathione.

CLA is a precursor of arachidonic acid (AA). AA is a polyunsaturated fatty acid possessing 20 carbon atoms and four double bonds (C20:4) and is formed from linoleic acid (C18:2) by adding two carbons to the chain and further desaturation [21]. AA is an essential fatty acid and a precursor in the biosynthesis of anti-inflammatory prostaglandin E2: the conversion of CLA *in vivo* on the skin to PGE2 is triggered by skin oxygen and Glutathione (GSH) [22] itself, which has been directly linked to CLA to increase its effectiveness. The CLA-GSH system is also and above all used for anti-inflam-aging purposes, i.e., anti-aging linked to the action on micro skin inflammations that stress the skin. During the aging process, many physiological changes occur in the human body. Investigating the cellular and molecular mechanism underlying the inflammatory and the immune response has provided convincing evidence that up-regulated cyclooxygenase (COX)-2 and its product, particularly prostaglandin PGE2, play a critical role in the age-associated dysregulation of the immune and inflammatory responses

[23]. CLA, therefore, extinguishes the micro-inflammations that exacerbate the phenomenon of skin aging. Commonly, the cosmetic formula contains ingredients with soothing and anti-inflammation activity [24] because it is essential to recover damaged skin before facing the complex aging process.

The repairing action of the damaged skin can be exerted on hemidesmosomes or adhesion proteins between the basal surface of the keratinocytes or fibroblasts with the underlying layers.

Six hemidesmosome proteins are assembled in large clusters on the basal side of the cells. These multiprotein complexes provide firm adhesion of the epithelial cells to the membrane ground. The anchoring of the basement cells to the basement membrane is of fundamental importance for maintaining the integrity of the epithelial tissues. For example, in the skin, hemidesmosomes are crucial for the stable adhesion of the epidermis to the underlying dermis; therefore, mutations in the components of these adhesion complexes cause tissue fragility and blistering of the skin.

Integrin α6β4 is the central component of hemidesmosomes and is essential for their efficient assembly. The integrin forms a bond between its extracellular ligand laminin-5 and the internal plaque proteins plectin and BP230. Plectin and BP230 are members of the plakin family of cytoskeletal link proteins. Plectin and BP230 are bridges between the outer plaque and the intermediate filament system, where the hemidesmosome is attached [25]. The skin is a dynamic tissue that is constantly renewed, and therefore the assembly and disassembly of hemidesmosomes must be strictly regulated. When basal epidermal cells differentiate and move upward, the expression of integrin α6β4 is downregulated, and the hemidesmosomes are disassembled. Also, during skin wound healing, stable hemidesmosome adhesions must be weakened to allow basal keratinocytes to migrate to the wound site and reestablish the epidermis.

Hemidesmosome assembly and disassembly are essential not only for the proper functioning of normal cells; even in cancer cells, hemidesmosomes are disassembled to allow invasion into surrounding tissues [26]. During skin aging and photoaging, the number of hemidesmosomes decreases. Therefore, the skin barrier function deteriorates, becoming more fragile. The changes in hemidesmosome proteins in young and old skin were evaluated. It was found that the gene expression of some hemidesmosome proteins (dystonin, plectin, collagen 17A1, a, and integrins b) significantly decreased in old compared to young skin. These changes may be accompanied by reduced skin barrier function and the skin fragility of aged skin [27].

The interaction of the peptide with the receptor target involves the signaling of kinases pELK, RSK2, and pERK ½, which causes the disassembly of the hemidesmosome structure. In this way, the migration of cells previously anchored by the hemidesmosome is favored to repair cellular damage and regenerate injured tissues. Therefore, the hemidesmosome is a chain that holds the cells still in their position. The investigated peptide can dissolve the chains and favor the migration of the cell towards the damaged skin areas where its presence is required to heal tissue wounds [22].

Peptilift allows more significant healing of the injured skin by causing the disassembly of the hemidesmosome structure. Therefore, it also contributes to obtaining a more toned and healthy skin effect.

The present study evaluated a cosmetic formula's lifting and firming effect with 4% $_{w/w}$ Peptilift compared to Placebo. We measured instrumentally and with photographic images the product efficacy after two and four weeks of treatment to verify the ability of Peptilift to reduce wrinkle-lifting as a cosmetic ingredient for wellbeing. This work is part of a project whose goals are the research of endorphin peptides several topical applications that can be conveyed in cosmetic formulations without the need for medical intervention.

Study design

This randomized, single-blind comparative study was performed at the RD Cosmetics (Research and Development Lab on Cosmetic product) located in the Pharmacy Department, University on Naples Federico II, Naples, Italy.

The study was carried out in compliance with the quality assurance system requirements, according to the principles of Good Clinical Practices (ICH E6) and the principles established by the World Medical Association in the Declaration of Helsinki.

The study aimed to evaluate the lifting and firming effect of the new cosmetic endorphin peptide (Peptilift, Kalichem Srl, Rezzato – Italy) after 4-week treatment on healthy human subjects. The product's effectiveness should be objectively demonstrated by the significant decrease of cutaneous roughness values (Volume and Area) and the evident decrease of photoaging skin signs (more toned, elastic, hydrated, and compact skin).

The cosmetic-clinical trial set to evaluate Peptilifit efficacy involved forty women, Caucasian race, aged 40-65 years and with signs of skin aging on their face. These subjects were selected randomly from a general panel and divided into two groups, with 20 panelists for each one. The first group received Peptilift cream, the second one a Placebo as a comparison group.

Materials and Methods

Test product

The test product is a lifting moisturizing, firming cream manufactured by Kalichem Srl (Italy) containing the active ingredient Glutathione-CLA-SH_Pentapeptide-5 at 4% w/w. The cream used as a control (placebo) presented the same composition without the investigated peptide. Ingredients of test and control creams are listed in **Table 1**.

Study population

The research lab has a constantly renewed general panel of volunteers. Subjects come from all social categories and participate spontaneously in the tests. Before their

Table 1. *List of ingredients of test cream (Peptilift cream).*

Test cream (Peptilift cream): lifting moisturizing, firming cream, with luxury texture
Aqua, Sodium olivoyl glutamate, Cetearyl alcohol, Glyceryl stearate, Simmondsia chinensis seed oil, Coco caprylate, Dicaprylyl carbonate, Sh-Pentapeptide-5, Dimethicone, Glycerin, Disodium EDTA, Xanthan gum, Hydroxyethylacrylate taurate copolymer, Polyisobutene, PEG7, Paraben/Phenoxyethanol, Lactic acid, Parfum.

enrollment, test subjects received an objective evaluation using standardized numerical scales, i.e., they were subjected to CSI (Complete Skin Investigation, C+K electronic GmbH) analysis to assess their skin aging degree and skin type.

For the study, volunteers were selected by this general group based on the study's specific inclusion and non-inclusion criteria and their ability to comply with protocol constraints. The number of panelists who complied with the protocol without any significant change, which could influence the study results, had to be at least 40.

From this panel, forty healthy Caucasian subjects aged 40 - 65 years with signs of aging were enrolled. Critical exclusion criteria included: treatment with Botox (any serotype) in the facial area, any facial cosmetic procedure, or any biodegradable filler in the face within the past 12 months; any previous insertion of permanent material in the face; and planned cosmetic treatment of the face during the study period.

Treatment

Subjects were randomized to receive the Peptilift cream or Placebo on day 1. Then, they had to apply the product twice per day (morning and evening) after cleansing, massaging till absorption. Panelists are made "blind" to their group affiliation.

Bioinstrumental skin parameters detection

Wrinkles photography: At every checkup, wrinkle images and their numerical values were recorded using Visioface® 1000D (C+K electronic GmbH), which quantifies the wrinkles volume and area percentage variation and compares the images before after treatment. The camera takes high-resolution facial photos with standardized light and position. It analyzes facial changes such as volume, area, and depth of wrinkles, quantifying them.

Transepidermal water loss: The skin barrier function of the stratum corneum (SC) was measured by Tewameter® TM 300 (C+K electronic GmbH). Its open chamber principle measures the total amount of water lost from the dermal and epidermal tissues to the external environment through the SC.

The evaporation rate value was expressed in g/m²/h. Three assessments were performed on the external side of each cheekbone. The smaller is the TEWL, the more the skin barrier is intact.

Skin hydration: Skin hydration was determined on each cheekbone by measuring the capacitance of a dielectric medium, which is the SC (with increasing hydration, the SC dielectric properties change) through a Corneometer® CM 825 (C+K electronic GmbH). The average value (Water content, WC) of 5 assessments was registered.

Skin visco-elastic properties: The skin's overall elasticity and firmness through Cutometer® MPA 580 were measured. The probe acts as a suction/elongation method with subsequent skin releases. The resistance of the skin to the negative pressure (firmness) and its ability to return to its original position (elasticity) are displayed as curves (penetration depth in mm/time) in real-time during the measurement. From these curves, various interesting parameters, like R_0 and R_2, which variations are related to the product's pliability/firming and elasticizing capacity on the skin.

Self-assessment: At the end of the test period, panelists completed a self-assessment questionnaire on the product's subjective efficacy, as reported in **Table 2**.

Statistics

Checkup readings were considered at the enrollment day (D1), after 14 and 28 days (D14 and D28). The student's t-test was used to assess the differences between the average value; the significance level was set for $p < 0.05$. The average value and standard deviations were calculated for the baseline and every instrumental efficacy endpoint by setting with a spreadsheet:

D1 = baseline skin parameters values

D14 = average skin parameters values after 2 weeks of treatment

D28 = average skin parameters values after 4 weeks of treatment

D14 – D1 = average variation after 2 weeks

D28 – D1 = average variation after 4 weeks.

This difference is also reported as a relative percentage of variation (RV%).

Results

We included 40 healthy participants in this study. Test and control creams were well tolerated. A significant difference was observed between test and control creams for all parameters studied.

The Peptilift-treated panelists' skin characteristics were varied after treatment. Skin TEWL was lower two and four weeks after using the cream with the investigated peptide (D14: - 9.6%; D28: - 9.5%), compared with Placebo, which shows no statistically significant results. Moreover, there is an increase in TEWL values. The water content was also higher in panelists treated with SH-Pentapeptide-5 at $4\%_{w/w}$ compared with control (D14: + 16.7%; D28: + 15.5%). The SC water content and TEWL values resumed in Table 3 reflected a significant moisturizing action on the skin exercised by Peptilift **Table 3**.

Furthermore, overall skin elasticity and firmness increased proportionally to longer Peptilift-treatment. Changes in skin firmness (R_0) and elasticity (R_2) occur between peptide topical treatment and Placebo after two and four weeks (Table 4). The skin is firmer and more elastic in subjects treated with the

Table 2. *Self-assessment questionnaire.*

Nr.	Question
1	Do you feel a perception of well-being after cream application?
2	Do you feel more hydrated skin?
3	Do you feel a more toned and lifted skin?
4	Are your wrinkles less visible?
5	Do you feel your skin plumped?

Table 3. *Moisturizing efficacy of the tested creams.*

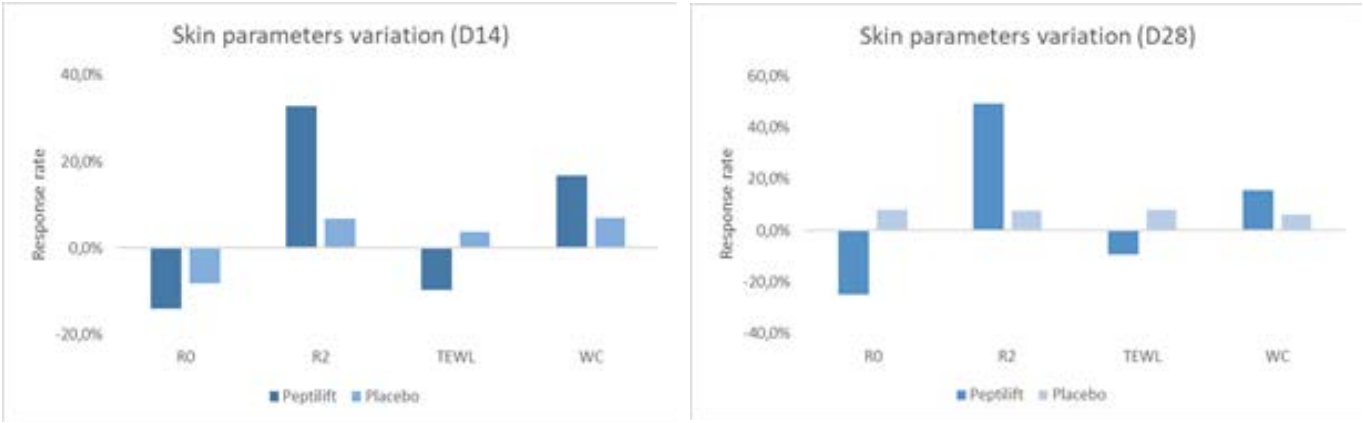
Skin parameter	Peptilift cream			Placebo		
	D1	D14	D28	D1	D14	D28
TEWL g/hm	12.5 ± 2.7	10.8 ± 2.5 *	10.8 ± 2.3 *	14.2 ± 3.8	14.3 ± 2.7	15.3 ± 6.1
Water content A.U	56.9 ± 12.6	65.6 ± 13.4 *	64.8 ± 11.9 *	62.8 ± 10.2	65.2 ± 12.6	64.3 ± 13.6

*(*p<0.05, **p<0.005, ***p<0.001)*

Table 4. *Skin visco-elastic property during 4-week treatment with the tested creams.*

	Peptilift cream			Placebo		
Skin parameter	D1	D14	D28	D1	D14	D28
R0 Mm	0.095 ± .041	0.082 ± .037	0.072 ± .032	0.098 ± .062	0.090 ± .033	0.106 ± .049
R2	0.533 ± .142	0.640 ± .133	0.665 ± 0.156	0.599 ± .160	0.617 ± .119	0.628 ± .142

*(*p<0.05, **p<0.005, ***p<0.001)*



1a) **1b)**

Figure 1. *Response rate (%) from baseline (D1) on the Facial skin parameters at two efficacy endpoints. a) 2-week checkup (D14), b) 4-week checkup (D28). (*p<0.05, **p<0.005, ***p<0.001)*

SH-Pentapeptide-5, indicating the product's ability to improve skin aging-related concerns, like dermis relaxation, atrophy of the skin layers, and elastosis **Table 4** [28].

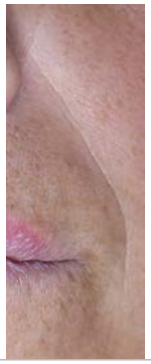
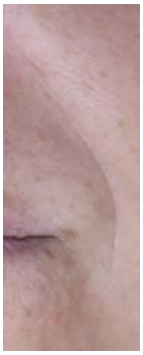
As a result, there were significant differences in the aged skin recovery ability between the Peptilift-treated and Placebo groups after two and four weeks. (Figure 1). High-resolution digital images were captured for all subjects at baseline and after 4 weeks of treatment. Representative examples of some subjects are shown in **Table 5**.

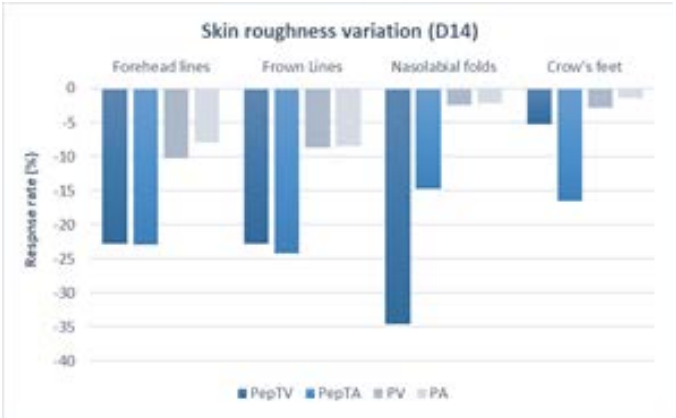
Volunteers showed moderate to severe skin roughness before treatment, which population disappeared after topic treatment with the SH-Pentapeptide-5. At D28, roughness and texture improved with mild levels (p = .0203) **Table 5**.

Visual grading analysis demonstrated that after test cream peptide treatment, a significant improvement of face roughness was observed. The numerical skin roughness analysis corroborated the visually lifting action. The Botox-like effect for endorphin-like action determines a hyperpolarizing effect on the presynaptic neuron. This hyperpolarization inhibits the acetylcholine release inhibiting muscle excitability. As a result, the mimic muscle relaxes, and the expression lines volume and area statistically decrease. (**Figure 2**)

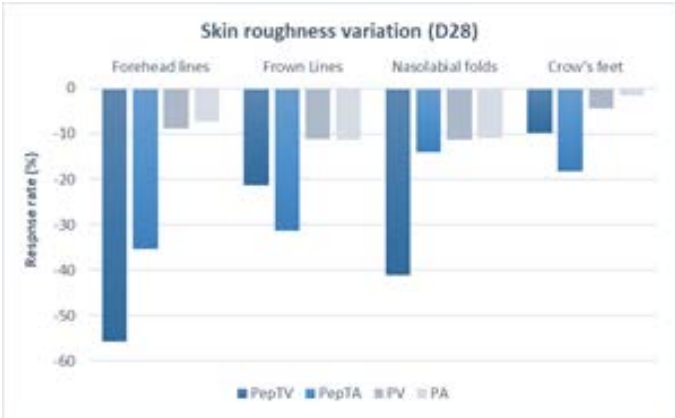
Results of the self-assessment questionnaire showed that Peptilift cream was significantly positive (**Figure 3**). Subjects considered their facial skin roughness less visible, more hydrated, toned, and lifted after 4-week Peptilift application **Figure 3**. The questionnaire revealed self-perceived benefits consistent with instrumental visual grading.

Table 5. *Representative images of the forehead and frown lines, nasolabial folds, and crow's feet of some panelists before (D1) and after the 4-week treatment (D28) with Peptilift cream.*

Peptilift-cream lifting efficacy	
D_1	D_{28}
	
	
	
	



2a)



2b)

Figure 2. *Response rate (%) from baseline (D1) on the Face skin roughness at two efficacy endpoints. a) 2-week checkup (D14), b) 4-week checkup (D28); PepTV and PepTA are respectively volume and area percentage variation in Peptilift Treated subject. PV and PA are volume and area percentage variations detected in the Placebo group.*

*(*p<0.05, **p<0.005, ***p<0.001)*

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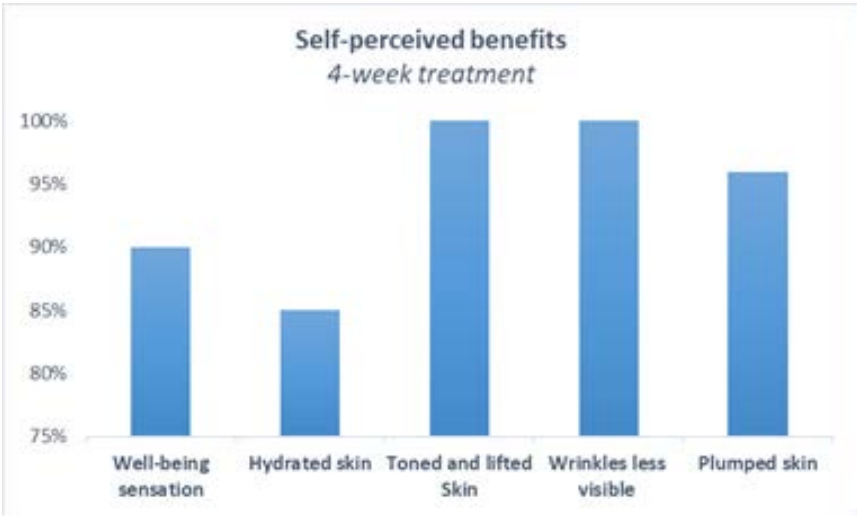

Figure 3. *Significant Results of self-assessment questionnaire after 4-week treatment with Peptilift cream.*

Discussion

Dermatological cosmetics offer topical formulas "lifting effect" or "botox like," which take their cue from aesthetic medicine, which global market is expected to grow to $58.34 billion in 2028 [29].

Cosmeceuticals combine cosmetics and pharmaceuticals; this field is nowadays a highly investigated research area. Because the scientific evidence, the clinical ones, are currently modest, this study aimed to provide an objective and reliable protocol to prove their activity in vivo. The use of bioactive peptides in the cosmetic field is becoming increasingly important. There are not only aesthetic touch-ups to improve one's appearance, but dermatological cosmetics, defined as cosmeceuticals, can do a lot. These are topical formulas, which have more than usual creams as they contain effective active ingredients that ensure rapid response times and a very natural result without causing annoying side effects. These hi-tech formulas are characterized by high concentrations of active ingredients that effectively counteract the appearance of wrinkles.

Interesting bioactive cosmeceutical group ingredients are peptides, which due to their properties, meet most of the requirements presented by the cosmeceutical industry when composing new formulas. Peptilift development occurs in this context; its aa sequence, active as anti-aging peptides, has been structurally modified over time to achieve new physicochemical properties. The developed SH-Pentapeptide-5, Peptilift, is an endorphin peptide associated with a delivery system based on Conjugated Linoleic Acid (CLA) amidified with Glutathione. This innovative technological formulation carried out noticeable actions when applied daily topically.

The experimental study carried out on subjects showing signs of skin aging, the application of Peptilift Cream (with 4%$_{w/w}$ SH-Pentapeptide-5) daily for one month, exhibit a significant statistical decrease in the main expression lines, an increase in skin elasticity and firmness, and an improvement in the hydration profile and skin barrier recovery.

These results suggest that Peptilift tested on 20 female panelists aged 40 - 65 years can plump and firm the skin and reduce mimic and gravitational wrinkles, for which it has an excellent anti-aging capacity. The action was demonstrated to the corresponding single-blind Placebo cream, also tested on 20 volunteers, which, on the other hand, did not show significant improvement in the skin parameters under observation.

The peptide carries out its beneficial action through a complex mechanism of action articulated on three levels. The primary soothing action occurs because CLA is a precursor of the anti-inflammatory PGE2 that gives an anti-aging effect linked to the micro skin inflammations relief. The secondary damaged skin restoration occurs through the hemidesmosome chains disassembly, favoring cell migration towards damaged skin areas to heal tissue wounds. Finally, a botox-like effect for endorphin-like action is obtained because the peptide acts on the neuromuscular synaptic junction in the facial muscles. Interaction with its target, δ-opioid receptor, determines a hyperpolarizing effect on the presynaptic neuron. This hyperpolarization inhibits the Ach release; in this way, muscle excitability is inhibited. As a result, the mimic muscle relaxes, and the expression lines are less visible. This synergic action made Glutathione-CLA-SH-Pentapeptide-5 (Peptilift) a promising ally in treating typical aging and stress-related dysfunctions.

Conclusions

Peptilift is a cosmeceutical ingredient with impressive lifting and firming action. Moreover, it ameliorated epidermal barrier function and increased skin water content, demonstrating its potential effect as a dermo-cosmetic ingredient in alleviating critical conditions related to the aging process. In contrast with other peptides like the botulinum toxin, this system is not an injective treatment; consequently, avoiding the not appreciated side effects, and in addition, it can be conveyed in home-daily remedy without the need for medical intervention.

Abbreviations

AA arachidonic acid; aa amino acids; CLA conjugated linoleic acid; GSH glutathione; PGE2 prostaglandin E2; SC stratum corneum; TEWL transepidermal water loss; WC water content; Ach acetylcholine.

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Conflict of interest

The authors declare no conflict of interest.

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