

# Snake Venom Peptides Use In Anti-Ageing Products

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## 1. Introduction

- 1) The cosmetic industry requires a variety of different ingredients for skin care products. These include peptides, growth factors, antioxidants, anti-inflammatory botanicals, and polysaccharides. As these products show drug-like effects they are commonly referred to as cosmeceuticals.
- 2) Originally, peptides became of interest in cosmetics as a result of the discovery of their beneficial effects in wound healing. As peptides are involved in an immense number of physiological processes, it was logical to further exploit them for cosmetic applications.
- 3) Most of the peptides used in cosmetics are designed to counteract the aging process of the skin. The need for such products is driven by the increasing desire in modern society to maintain a young appearance even at an older age, and the breadth of possible treatments to achieve this goal.
- 4) The increasing knowledge about the molecular details of the skin-related aging processes has significantly contributed to the exploration of novel anti-aging agents.
- 5) Snake have been used medicinally the since 19 th Century.
- 6) Snake are not directly used in medicine and Personal care Products to Peptide extract from snake venom and then it is used.

## Types of Peptides

Peptides have become very important ingredients in cosmetic products, especially in anti-aging preparations. According to their mode of action, they have been divided into three main groups:

- 1) Signal Peptides
- 2) Neurotransmitters- affecting Peptides
- 3) Carrier Peptides



## 1) Signal Peptides

Aged skin is, amongst others, characterized by reduced levels of collagen and elastin. Increasing the number of fibroblasts or their collagen production and/or inhibiting further collagen hydrolysis are therefore considered effective means to halt or slow the aging process of the skin.

Many of the peptides used in cosmetic preparations are compounds which act on fibroblasts. One of the peptides described to act in this way is H-Val- Gly-Val-Ala-Pro-Gly-OH (VGVAPG) (Product: H-2390 Chemotactic Domain of Elastin)

H-2390 is an elastin-derived peptide sequence repeated several times in tropoelastin. It was found to stimulate the proliferation of human skin fibroblasts presumably via the elastin receptor.

The N-terminally palmitoylated peptide is marketed under the name of palmitoyl oligopeptide and is supposed to penetrate more efficiently through the epidermis than the parent compound.

## 2) Neurotransmitter-affecting Peptides

Many of the peptides used in cosmetic preparations belong to the group of neurotransmitter-affecting peptides. These peptides act in a similar way as botulinum toxin (Botox).

Inhibiting signal transduction pathways at neuromuscular junctions they attenuate the formation of wrinkles and fine lines which appear over time due to the repetitive contraction of the intrinsic muscles of facial expression.

Botulinum toxin, synthesized by the bacterium *Clostridium botulinum*, is the most potent toxin known. It is a disulfide linked heterodimer consisting of a heavy and a light chain.

Upon binding to the peripheral neuronal presynaptic membrane mediated by the heavy chain the toxin is internalized by receptor-mediated endocytosis.

After translocation from the endocytotic vesicle into the cytoplasm, the light chain proteolytically cleaves either SNAP-25 or synaptobrevin depending on the serological subtype of the neurotoxin.

## 3) Carrier Peptides

The tripeptide H-Gly-His-Lys-OH (GHK) (Product: H-3510 Liver Cell Growth Factor) was originally identified in human plasma and has a high affinity for copper<sup>2+</sup> (Cu<sup>2+</sup>). It acts as a signaling peptide and a carrier

molecule for copper which is a co-factor for several enzymes involved in collagen and elastin formation.

The copper peptide was shown to stimulate wound healing but also to reduce fine lines and wrinkles and to improve elasticity and firmness of aged skin. A wide variety of effects have been described to GHK-Cu.

The peptide exhibits anti-inflammatory actions by suppressing the expression of proinflammatory cytokines. It also chemoattracts capillary cells, macrophages and mast cells, increases the synthesis of collagen and elastin, and stimulates the proliferation of fibroblast and keratinocytes.



## 2. Benefits of Snake Venom Peptide Cream

- Advanced wrinkle reduction
- Proven to revitalize, replenish and moisturize your skin. Fight back against the signs of aging, wrinkles & fine lines
- All-in-one solution for smoother and more even looking tone
- Helps to reduce the visible effects of sun damage
- Unified solution for firmer and ageless glow
- Promotes a flawless beautiful appearance
- Lift skin to youthful glow
- Nourish away the dryness
- Optimize collagen production
- Reduce the appearance of dark circles and Revitalizes and regenerates the skin.



## 3. Factors Contributing to Aging

- The Sun: Prolonged exposure to it causes a very high percentage of problems that are associated with aging. The UV radiation from the sun and especially UVA, are destroying the elastin and collagen in the skin, and accelerate the production of melanin, which results in the appearance of blemishes and wrinkles.
- Pollution and environmental temperature changes: The exposure of our skin with a contaminated environment covers it with a layer of dirt that ends up clogging the pores and preventing oxygen from reaching cells. Also, move to other areas with heating, air conditioning requires the skin to be in a continuous cycle of dryness and moisture that ends up affecting it negatively.
- Smoking: The problems' arising from this bad habit is numerous, destroys the collagen in the skin, reduces the ability of healing. The nicotine in cigarettes reduces the diameter of blood vessels, which prevents blood from reaching the blood vessels normally until the top layer of skin so that wrinkles appear prematurely and the skin acquires a yellowish color.
- Stress and Insomnia: Having situations or periods of stress, no doubt, ultimately affects the skin, reflected in the appearance of spots, dryness, and excess fat. Plenty of sleep is also necessary for the skin to refresh itself.



## 4. Viper Snake Venom Anti-aging Serum

- It is the best eye wrinkle serum to erase wrinkles and eliminate eye puffiness.
- Snake Venom Anti-wrinkle Serum would be a potent, powerful, natural anti-aging cream by itself
- Is the best of all anti-aging creams
- Anti aging rejuvenating facial cream for all skin types
- Firms Sagging skin
- Encourages the formation of new cells
- Helps in skin rejuvenation
- Peeling off of dead skin to reveal new cells underneath
- Removes deep facial wrinkles.



## 5. Skin Ageing

The aging process begins when we enter the world and the effects of aging are evident in our bodies throughout our lives. Beginning in our 20's, the signs of aging start to become noticeable.

Genetically programmed chronologic aging causes changes in collagen and elastin, the connective tissues that supply firmness and elasticity to the skin.

The genetic program of individuals is different, so the loss of skin firmness and elasticity occurs at different rates and different times in one individual as compared to another.

As skin becomes less elastic, it also becomes drier and underlying fat padding begins to disappear. With the loss of underlying support by fat padding and connective tissues, the skin begins to sag; it appears less supple and wrinkles form.

Skin aging is a process influenced by extrinsic and intrinsic factors and is manifested by a progressive loss of skin tissue, the gradual loss of skin elasticity, and the appearance of fine lines and wrinkles.

The premature skin-aging effects of tobacco smoking are caused by induction of collagenase activity and the reduced blood flow to the skin due to nicotine-induced vasoconstriction.

Intrinsic factors such as the generation of ROS contribute to the loss of extracellular matrix proteins, a decrease in cutaneous blood flow, and a loss of cells and cell function.

## 6. Syn-Ake

Syn-ake is an anti-wrinkle material based on a synthetic tripeptide that "mimics" the effects of a peptide found in the venom of the Temple Viper snake.

It was created by Pentapharm Ltd, a Swiss based chemical company. Reportedly, they are the largest snake breeders and keepers in the world too.

SYN®-AKE is an effective wrinkle smoothing compound based on a synthetic tripeptide that mimics the effect of

Waglerin 1, a peptide found in the venom of the Temple Viper, *Tropidolaemus wagleri*.

SYN®-AKE helps to smoothen the appearance of expression lines. DSM has developed, over the past 30 years, a unique approach for the breeding and housing of venomous snakes whose venom is used for therapeutic (anticoagulants, haemostatics) and diagnostic products.

The Temple Viper's hunting method makes use of the venom protein Waglerin 1, which has a strong muscle-relaxing effect.

The tripeptide SYN®-AKE mimics the essential amino acid sequence of this functionality. SYN®-AKE's activity is attenuated compared to Waglerin 1 and has been thoroughly tested.

It is a safe, effective, and painless cosmetic alternative to controversially discussed muscle-relaxing anti-aging treatments like botulinum toxin.

## 7. Mechanism of Syn-Ake

Syn-ake is designed to work much like Botox, which reduces muscular contractions in the face and reduces cell movement; thereby keeping the skin smooth. The concept behind Syn-ake is that since snake venom causes muscular paralysis, a synthetic derivative of the venom would work to temporarily deaden the muscles in the face to prevent the formation or deepening of wrinkles.

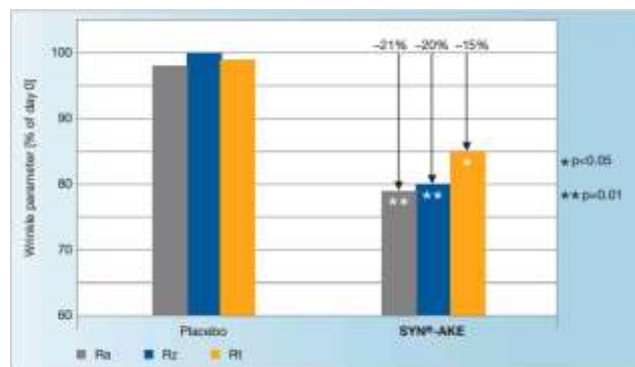
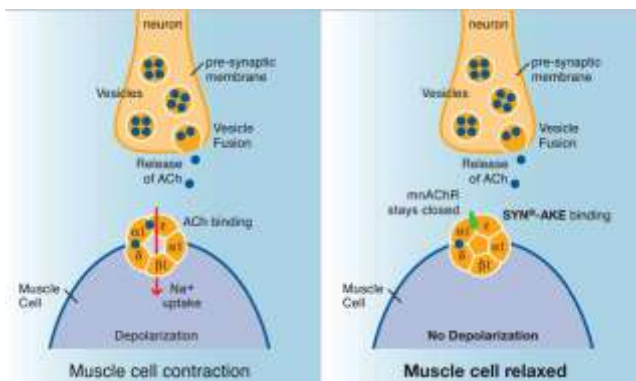
Wrinkles around the eyes and mouth form over time because the muscles in the face contract in repeated motions that cause you to smile, laugh, and frown. These facial expressions cause the skin to stretch and wrinkle each time, and eventually, lines and wrinkles form because your skin loses its elasticity and can no longer snap back to its original position.

Syn-ake can be applied to wrinkles on the forehead, the neck, around the mouth, and around the eyes, although extreme care should be taken to keep the product out of the eyes.

Much like Botox injections, the effects of Syn-ake fade over time and are not a permanent solution to fighting wrinkles.

In the chemical sell sheet, data is presented from 2 studies. The first suggests that Syn-ake can reduce muscle cell contractions in a laboratory test. That's not in people but in a cell culture of muscle cells.

The second study shows that after 28 days of using a Syn-ake laced cream, you get a shrinkage of up to 52% of wrinkle.



### Functions

- SYN@-AKE is an excellent wrinkle smoothing compound.
- Smoothes the appearance of mimic wrinkles in a short period of time.

### Properties

- Reversible antagonist of the muscle nicotinic acetylcholine receptor (mAChR)
- Blocks Na<sup>+</sup> uptake at the postsynaptic membrane
- Attenuates muscle cell contractions
- Fast acting

### Cosmetic Applications

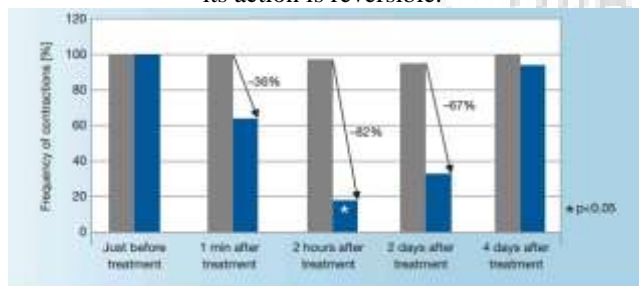
- Age-defying effect particularly effective against expression lines
- Intensive wrinkle smoothing care.

## 8. Efficacy Tests

### In Vitro

The efficacy of the SYN@-AKE tripeptide (0.5 mM) has been demonstrated in vitro by measuring the frequency of contraction of the innervated muscle cells as a function of the incubation time.

SYN@-AKE peptide reduces muscle cell contraction and its action is reversible.



### In Vivo

The measurement of the wrinkle smoothing effect of SYN@-AKE (4%) was compared to a placebo. A cream was applied to the forehead twice daily for 28 days. The study included 15 volunteers per group (age 40–60).

SYN@-AKE – Age-Defying Effect. The smoothing effect (reduced Ra) was measured on 80% of the volunteers and reducing the appearance of wrinkles was (reduced Rz and Rt) measured on 73% of the volunteers.

Result show up to 52% reduction in the appearance of wrinkle size after 28 days application.

### The SYN@-Peptides Portfolio

Proteins and peptides play an important role in the beauty of skin as structural components such as collagen, elastin and laminin, and as inhibitors and stimulating agents such as growth factors like TGF- $\beta$  or regulators of biochemical process. The design of SYN@-Peptides is inspired by naturally-occurring proteins and peptides.

Our state-of-the-art peptide synthesis technologies allow tailor-made modification to mimic natural peptide activity. to their activity and stability, SYN@-Peptides help to maximize the value of cosmetic formulations.

We use our bright science to develop very small-sized but potent tri- and tetra-peptides that are more likely to ensure visible, targeted effects. Their increasing success is based on the fact that they are trusted as biologically-active ingredients and that they perfectly fit consumer desires for powerful ingredients based on scientific breakthroughs.

Our entire SYN@-Peptides range is offered in a stable glycerin/water base with no additional preservative system. This allows broad application in most cosmetic formulas at the low level of 1 to 4%. Each SYN@-Peptide is claim-substantiated based on thorough in vitro and in vivo study results

#### 1) SYN@-TACKS

##### For firm and compact skin

A well-folded dermal-epidermal junction (DEJ) is the basis for healthy, firm skin. As we get older, the DEJ becomes flatter and less well organized, Resulting in wrinkles and other signs of aging. SYN@-TACKS restores DEJ function by boosting the synthesis of hemidesmosomal proteins. It increases elasticity, firmness and suppleness, so that skin looks and feels younger within weeks.

#### 2) SYN@-COLL

##### Reverse visible signs of photo-aging in just 4 weeks

SYN@-COLL – a small molecular synthetic peptide – has been designed to prevent the formation of wrinkles and to

reduce their appearance. The SYN®-COLL molecule has a dual effect. Firstly, it boosts collagen by mimicking the human body's own mechanism to activate latent transforming growth factor beta, TGF- $\beta$  (Tissue Growth Factor), a key element in the synthesis of collagen. It also protects collagen from degradation through the inhibition of matrix metalloproteinases (MMP). Both activities work synergistically to maintain complete structural integrity of the skin.

### 3) SYN®-HYCAN

**For contour remodeling** Loss of skin firmness is one of the very visible signs of aging. SYN®-HYCAN helps fight skin sagging by boosting hyaluronan content in the skin. The tripeptide also increases the expression of decorin and lumican, two important proteoglycans, which support the formation of new collagen fibrils and increase their quality and strength. Fresh hyaluronan and stronger collagen fibrils result in a visible remodeling effect.

### 4) SYN®-AKE

#### For expression lines

Facial expressions are part and parcel of daily communication. Young skin is resilient to involuntary muscle contractions of the face, but older skin develops expression lines, such as crow's feet and forehead wrinkles. Let your face relax without losing the ability to express yourself. SYN®-AKE's effect reduces the appearance wrinkles, and is fast acting, long-lasting and fully reversible.

### 5) SYN®-TC

#### For smooth skin

SYN®-TC is a synthetic peptide-based complex, tailor-made to ensure best performance for high performing, facial anti-ageing formulas. It significantly increases the formation of Collagen I, III, IV, VII and XVII to facilitate their unique contribution to beautiful, smooth skin. In a comprehensive study, consumers confirmed they experienced a new dimension of skin smoothing. In only 28 days at a usage level of 2.5%, skin becomes smoother with a softer touch and an improved overall young-looking appearance.



#### Marketed products

- Dermalux® (Rapid Wrinkle Reduction)
- VENIN ROYALE
- Nuage Skin
- Vivlux Skin Care.



## 9. Conclusions

Synthetic peptides have become important for the cosmetic industry. Due to demographic changes and the aging population wishing to maintain a young lifestyle and appearance, cosmetic industry research has focused on anti-aging skin therapy. Today, more than 25 peptides are used in anti-aging skin care products and there are many more in development.

Peptides and proteins play a significant role in cosmetic anti ageing as well as therapeutic applications such as wound healing, reducing excessive scarring, fibrosis, inflammation and to treat burns. With the advent of new technologies and new peptide drugs being developed, we are beginning to see promising signs of dermal regeneration, collagen and elastin synthesis, increased glycosaminoglycan, proteoglycan and fibronectin production as well as improved wound healing in vivo.

Effective formulation and topical delivery strategies are required to overcome the stratum corneum barrier and to properly release the active from the vehicles at the target site in sufficient quantities to exert an effect. Effective delivery approaches are available to enhance the dermal delivery of peptides including the use of elastic vehicles,

solid lipid based drug delivery systems, micro-emulsions and electro spun fibres.

Each method has advantages and drawbacks and its value depends on the vehicle, excipients and physicochemical characteristics of the peptide or protein used.

The development of 'one size fits all' peptide/protein-containing formulation is unlikely as each peptide becomes the subject of an individual case study. To gain optimal results a combination of these approaches may be utilized.

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