Chapter 2
Concentrates of biologically active ingredients

Using products containing high concentrations of active ingredients is another option for intensive treatment of healthy skin besides peels. Many of these products (just like peels) are multifunctional and allow several aesthetic problems to be solved simultaneously. They are often applied under the mask, creating an occlusion film and ensuring even more active penetration of ingredients through the *stratum corneum* already prepared by cleansing. In some cases, they can also be applied after peeling.

All ingredients discussed in the following sections can also be used in home care products but are usually found in lower concentrations.

2.1. Peptide regulators

The appearance of peptides in the cosmetic market made much noise — some called them a new milestone in cosmetic dermatology and skincare, others treated them with suspicion as just another advertisement. However, even their relatively short use has shown that peptides do not justify the hopes placed on them, although they may surprise us in the future. Even now, a separate niche in anti-aging medicine is occupied by so-called remodeling peptides, which start synthesizing extracellular matrix components. These myorelaxant peptides are considered an alternative to botulinum toxin, neurotransmitter peptides, and many compounds that improve microcirculation. In addition, new substances appear every year, their range of possibilities is expanding, production is becoming cheaper, and the availability of peptides in cosmetic products is increasing.

There is no doubt that peptide skincare products are a trend that will take the lead in aesthetic medicine for many years to come. Let's remember what peptides are and see what new products the cosmetic market offers today.

2.1.1. Basic properties

Peptides are a group of substances with molecules comprising amino acids linked together by peptide bonds. In other words, they are proteins in their chemical structure, but nowadays, they are divided into separate groups. Thus, **proteins** are those amino acid chains that consist of hundreds or more amino acids (for example, a collagen molecule includes about 500 amino acids), while **peptides** are short-chain structures containing only a few (up to tens) amino acid residues (**Fig. III-2-1**).

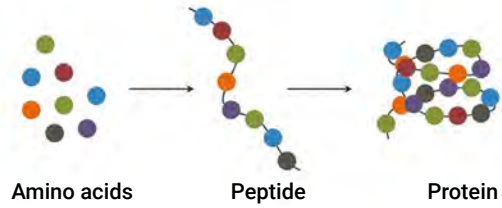

Figure III-2-1. Peptides and proteins

Although there are only 20 amino acids in our body, their sequence in the peptide chain can give rise to countless combinations. Since the sequence of amino acids determines the biological functions of peptides, the potential range of their uses is almost unlimited.

Peptides are particularly valuable for their ability to regulate various aspects of cellular activity. For example, most peptides are signaling molecules: by binding to cell receptors (in the "key-lock" manner), they can "switch" cell functions, triggering or blocking specific processes, such as the synthesis of key proteins of the extracellular matrix, keratinization, or melanogenesis (**Fig. III-2-2**). Since intercellular signaling systems were formed at the earliest stages of evolution, the "orders" encoded in peptides are universal. Human cells can be influenced by peptides from various animals and even plants. In addition, peptides can bind to individual proteins, thus blocking or stimulating their function.

In cosmetic chemistry, it is customary to indicate the number of amino acids that make up a peptide in its very name. For example,

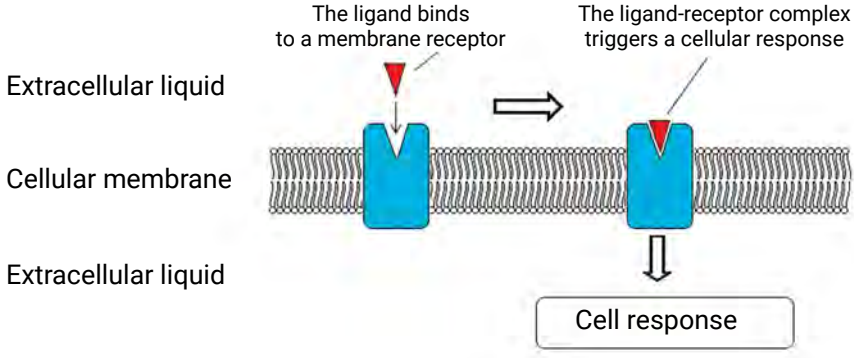

Figure III-2-2. The peptide interacts with the receptor on the cell membrane in the "key–lock" manner

a peptide consisting of two amino acids is called a dipeptide, those which contain three amino acids are called a tripeptide, etc. The most interesting prospects concern using peptides containing 2 to 10 amino acids. The small size of such peptides helps them move easily in the intercellular space and penetrate the skin. The classic rule of 500 Da says that the skin barrier limits the penetration of substances with a larger molecular weight. Since the mass of one amino acid is, on average, 100 Da, small peptides can pass through the *stratum corneum* without additional help (Bos J.D., Meinardi M.M., 2000). However, it should be noted that many peptides are water-soluble compounds, so they are "sewn" a lipophilic "tail" (most often palmitic acid), which facilitates the passage of the molecule through the lipid layers of the *stratum corneum* and is then "cut off" by special skin enzymes. Transdermal carriers (e.g., liposomes) or other permeability enhancers can also be used for this purpose (Bruno B.J. et al., 2013). In addition, peptides are shorter than proteins and do not form tertiary structures, which are very sensitive to external influences. This makes them easier to preserve in the composition of cosmetic products than larger proteins.

2.1.2. Types of cosmetic peptides

Many cosmetic peptides have been developed and divided into different groups according to the mechanisms and focus of their activities,

although they are most actively used in anti-aging procedures. The main groups and their already established and most popular representatives are listed below (Pai V.V. et al., 2017; Schagen S.K., 2017).

Remodeling peptides rejuvenate the composition of the extracellular matrix of the dermis by regulating the natural processes of formation and decay of its components. They can directly affect fibroblasts and thus activate the synthesis of dermal matrix components (matrikins, which are fragments of collagen and elastin and are a signal to fibroblasts that the extracellular matrix is being degraded) or act indirectly through stimulation of growth factors and other ways:

- Matrixyl (INCI: Palmitoyl Pentapeptide-3)
- Ascotide (INCI: Ascorbyl Pentapeptide-3)
- GHK tripeptide as lipoprotein (Dermaxyl et al.), in complex with copper (GHK-Cu), or pure GHK
- SynColl (INCI: Palmitoyl Tripeptide-5)
- Decorinyl (INCI: Tripeptide-10 Citrullin)

Homeostasis-stabilizing peptides activate the skin's own protective potential (including antioxidant protection):

- GHK-Cu (INCI: Prezatide Copper Acetate)
- Kollaren (INCI: Tripeptide-1)
- Peptamide (INCI: Hexapeptide-11)

Melanogenesis-regulating peptides can either enhance or attenuate melanin production mainly by activating or blocking receptors for α-melanocyte stimulating hormone (α-MSH):

- Melatim (INCI: Palmitoyl Tripeptide-30)
- Melitan (INCI: Acetyl Hexapeptide-1)
- Melanostatine (INCI: Nonapeptide-1)

Neurotransmitter peptides (opioid peptides) increase the threshold of skin sensitivity to various external influences (temperature, chemical, mechanical) through the release of opioid mediators and their effect on the cutaneous nerve endings:

- Calmosensine (INCI: Acetyl Dipeptide-1 Cetyl Ester)
- Skinasensil (INCI: Acetyl Tetrapeptide-15)

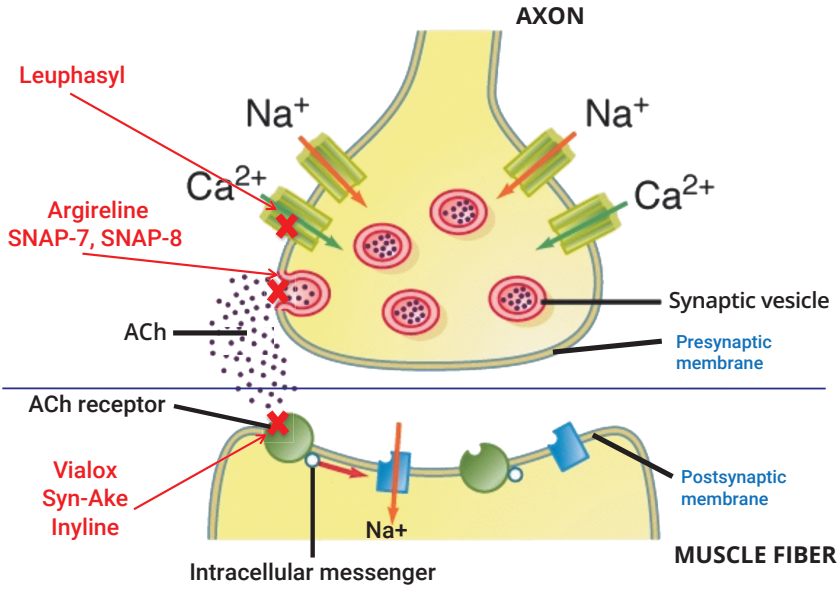

Figure III-2-3. Mechanisms of action of cosmetic myorelaxant peptides at different targets of nerve impulse transmission

The mediator acetylcholine (ACh) enters the synaptic cleft and binds to the acetylcholine receptor (ACh receptor) on the postsynaptic membrane of the muscle cell. This binding results in a release of an intracellular messenger in the muscle, which binds to the inside of the ion channel; the channel opens, and sodium ions enter the cell through it. The signal of muscle fiber contraction is an increase in the sodium ion concentration in the cytoplasm.

Myorelaxant peptides block acetylcholine receptors (in various ways) and thus prevent nerve impulse transmission and muscle fiber contraction (**Fig. III-2-3**). They do not paralyze the muscle like botulinum toxin but rather gently relax it:

- Argirelline (INCI: Acetyl Hexapeptide-3)
- SNAP-7 (INCI: Acetyl Glutamil Hexapeptide-1)
- Syn-Ake (INCI: Dipeptide Diamino Butyroyl Benzylamid Diacetate)
- Vilox (INCI: Pentapeptide-3)

Peptides that improve microcirculation and lymph flow regulate the permeability and improve the elasticity of the vascular wall, have an anti-edema effect, and activate microcirculation:

- Eyeseryl (Acetyl Tetrapeptide-5)

Peptides that act as activators of the antimicrobial peptide production stimulate the formation of their peptide molecules capable of destroying microbial cell membranes:

- Bodyfensine (INCI: Acetyl Dipeptide-3)

Peptides that act as immunomodulators regulate the skin's immune system by normalizing the balance between pro-inflammatory and anti-inflammatory cytokines:

- Rigin (INCI: Palmitoyl Tetrapeptide-3)

This is just a small subset of hundreds of cosmetic peptides. Every year new molecules with new properties are developed.

2.1.3. Growth factors

Growth factors are also conventionally referred to as peptide regulators, although they are larger than peptides. Growth factors belong to a group of cytokines — signaling molecules with the help of which cells send "messages" to each other. They constitute a special group of cytokines and are so named for their ability to stimulate living cell growth, proliferation, and/or differentiation. Due to this feature, growth factors are directly involved in physiological regeneration (natural tissue renewal) and reparation (tissue repair after damage).

The idea of using growth factors for the prevention and treatment of aging signs is based on the fact that, in the skin, even in the absence of visible damage, there are permanent processes of physiological renewal, and this supports its integrity and functional consistency. As a superficial organ, skin is constantly "targeted" by aggressive environmental factors and can be seriously damaged at any time. Therefore, the skin must be in a state of high readiness to repel external attacks and recover quickly after strikes. To do this, all its cellular and extracellular elements should be functional. This is possible due to the precise