Multifunctional Peptides

Peptides are fragments of proteins and, like proteins, they are made up of amino acids.

Amino Acids

Amino acids are the building blocks of peptides and proteins. They are small (molecular weight between 100 and 200 Daltons [1]) but biologically vital compounds containing an amino group (NH2) and a carboxylic acid group (COOH) as well as a side-chain structure that varies between different amino acids. While hundreds of amino acids are known, only twenty are coded for in human DNA and used by human cells to build proteins and peptides [2].

Peptides

When amine and carboxylic acid groups in amino acids join to form amide bonds, a peptide is formed. Peptides can be classified as oligopeptides and polypeptides. “Oligo” means “few” and refers to peptides with less than 20 amino acids in a chain. “Poly” means “many” and refers to peptides that contain up to 100 amino acids [3]. Peptides can also be named according to the number of amino acids in their chains. For example, a dipeptide contains 2 amino acids and a tripeptide contains 3 amino acids.

The primary function of most peptides is signalling, which means to bring a biochemical message from place A in the body to place B and effect an action there [1]. Some disturbance (internal or external) leads to the release of a small amount of peptide in a cell, in the blood, in a gland, in the brain or in some other organ; the peptide then travels through the body until it interacts with the target receptor (either on the cellular surface or, after having penetrated the cell wall, within the cell nucleus). This interaction or binding then triggers further activity at the site, destined to respond to and correct the initial disturbance [1].

Some well-known biological activities of peptides in the human body are: regulation of blood sugar concentration (eg. insulin), blood pressure regulation (eg. angiotensin), lactation and birthing (eg. oxytocin), diuresis (eg. vasopressin), pain reduction (eg. endorphins), tanning (eg. a-MSH) and free radical scavenging (eg. glutathione) [1].

A tissue protein, such as collagen, elastin or fibronectin, is broken into fragments by enzymatic hydrolysis, either during normal tissue renewal, or as a consequence of induced damage (eg. free radicals, mechanical wound). Various pieces of amino acid strings are generated, which when small enough, are readily available to act as “messengers” in the surrounding tissue, and will act as chemo-attractants, transport aids and stimulants to trigger neo-synthesis of the necessary tissue molecules to renew/repair the original structure [1].

Proteins

Scientists commonly differentiate between proteins and polypeptides based on their size and structure. Regarding size, a polypeptide composed of more than 100 amino acids is generally classified as a protein [1]. For instance, collagen has 1,000 amino acids and fibronectin contains 4,000 amino acids [2].

Proteins can be categorized by their function. There are structural proteins, such as collagen, elastin and fibronectin for building tissue. Enzymes are very specific proteins, which catalyze biochemical reactions, such as tyrosinase and superoxide dismutase (SOD). Transport proteins bind to a specific substrate and carry it through the body; for example, hemoglobin is as oxygen carrier and ferritin transports iron. There are many other functional proteins like antibodies, cytokines and coagulants [1].

Peptides in Skin Care

Peptides come in two forms: either they are synthesized as mixtures of protein fragments obtained by partial hydrolysis of collagen, elastin, keratin, wheat or other plant proteins; or they are synthesized one peptide link at a time until a well-defined chosen amino acid sequence is achieved [3].

The specific amino acid sequence determines the function of the peptide. For example, Gly-His-Lys stimulates collagen synthesis in fibroblasts [1] while Gly-His-Lys stimulates lipolysis in adiposites [4] (Note: His = Histidine, Lys = Lysine, Gly = Glycine) [1]. There are more than 1300 peptides listed in the INCI dictionary but only a few have widespread use and recognition [3].

Most peptides used in cosmetic products are biomimetic, meaning that they are identical or very similar in structure to those peptides we have in our skin and in our bodies. They have the same or very similar activity, thus mimicking the body’s biology [3].

Delivery of Peptides in the Skin

The stratum corneum is a lipophilic barrier, being only 13% water. Peptides are charged and hydrophilic which is an issue for skin penetration. Therefore, many peptide formulations contain penetration enhancers (eg. solvents, surfactants), delivery vehicles (eg. liposomes, nanoparticles) or modifications to the peptide (eg. palmitoylation) [3].

It has been shown that even small peptide molecules (like the dipeptide carnosine) are too hydrophilic and electrically charged to penetrate any further than the first or second layer of the stratum corneum. The larger the peptide (beyond six or seven amino acids), the less likely it is to go anywhere into the deeper layers of the skin [1].

Lintner & Peschard have shown, however, that the attachment of a lipophilic chain (fatty acid of sufficient length) to the smaller peptides can increase the penetration rate by a factor of 100 or more. It is important to note that the peptide still does not diffuse beyond the dermal layer; therefore, no uptake in blood or lymphatic fluids is to be expected and there is no systemic activity [1].

Antiaging Peptides

Collagen and elastin are two important extracellular matrix (ECM) proteins in the dermis. Degradation of the ECM occurs with age leading to decreased collagen, hyaluronic acid and other molecules. As a result, young smooth skin becomes wrinkled over time. When collagen breaks down, it forms peptide messengers, which interact with specific receptors to activate genes involved in the process of wound healing: fibroblast recruitment, cell proliferation, keratinocyte setting and anchoring, extracellular matrix synthesis and micro vascularization. Alternatively, peptides can stimulate collagen production by boosting certain growth factors like TGF-b [3].

History of Peptides in Skin Care

Synthetic peptides were first introduced in 1990. Initially acceptance was slow until the year 2000 when Sederma launched Matrixyl (palmitoyl pentapeptide-3 or PAL-KTTKS), which was the first peptide to be used in cosmetic formulations [3].

It was considered a breakthrough in the industry and, therefore, won the 25 Years of Innovation Award by In-Cosmetics, which recognizes the product that has had the most impact on the personal care market in the last quarter century. Peptides replaced topical animal collagen and elastin. Palmitoyl pentapeptide-3 is a synthetic peptide replica type 1 collagen fragment shown to stimulate type I collagen, type III collagen, and fibronectin [5,6].

After excellent results and tolerability in several anti-aging studies, the world adopted the peptide concept. Data was reported on close to 300 subjects participating in five independent clinical trials including one study that showed that palmitoyl pentapeptide-3 improved wrinkles with comparable efficacy to retinol without the irritation [1].

Copper Peptides

Copper peptide is a naturally occurring peptide with a strong affinity for copper. Copper is an antioxidant and cofactor for the enzyme lysyl oxidase involved in collagen synthesis [7].

In 1973, biochemist Loren Pickart isolated the copper peptide GHK from human plasma [8]. In 1977, David Schlesinger confirmed that the peptide isolated by Pickart was a glycyl-L-histidyl-L-lysine tripeptide. [7] Pickart found copper glycyl-L-histadyl-L-lysine (GHK-Cu) to be abundant in young people but reduced in older people. He then showed that GHK-Cu modulates various aspects of the wound-healing process, including chemo-attraction of immune cells, angiogenesis, and collagen synthesis [9-11]. Synthetic GHK-Cu is used as an anti-aging and reparative ingredient under the INCI name copper tripeptide-1 [12]

Neuropeptides

Neuropeptides are small proteinaceous substances produced and released by neurons through the regulated secretory route and acting on neural substrates [13].

Neuropeptide skin care focuses on how wrinkles are formed and uses neuropeptides to prevent and smooth wrinkles through blocking cell communication.

Some neuropeptides block transmission of signals from nerves to facial muscles. Argireline (acetyl hexapeptide-3), X-50 Myocept (Palmitoyl Hexapeptide-52, Palmitoyl Heptapeptide-18) and SYN®-AKE (Dipeptide Diaminobutyroyl Benzylamide Diacetate) work at the neuromuscular junction to decrease muscle contraction and smooth the overlying skin in a similar way to Botox®. However, it is doubtful that these ingredients could penetrate all the way through the skin to the level of the muscle in significant quantities to effectively block muscle contraction like Botox does.

Other Peptides?

Along with antiaging peptides, copper peptides and neuropeptides, there are many other peptides available in the skin care industry including lightening peptides, anti-inflammatory peptides, antioxidant peptides and antimicrobial peptides.

AlumierMD Uses a Selection of Peptides in Their Formulations Including the Following:

- **Matrixyl® synthe'6®:** Increases the production of 6 major constituents of the ECM and DEJ (dermal epidermal juntion) including collagen, elastin, fibronectin and hyaluronic acid.
- **Haloxyl®:** Formulated for under eye dark circles, Haloxyl® increases clearance of bilirubin and iron with an anti-inflammatory effect.
- **Eyeliss®:** Formulated for puffy eyelids, Eyeliss® contains a combination of 3 peptides that together increase lymphatic circulation, firmness and elasticity and decrease capillary permeability.
- **Glutathione:** An antioxidant peptide.
- **B-White®:** A TGF-ß biomimetic encapsulated peptide (lipsome) with inhibitory action on MITF to decrease skin pigmentation by decreasing key enzymes involved in pigmentation.
- **Dermal Rx:** A skin resurfacing oligopeptide.
- **Oligopeptide 10:** An antimicrobial peptide with excellent activity against P. acnes.
- **Oligopeptide 14:** An anti-inflammatory peptide that acts by down regulating IL-6 (interleukin-6) production in keratinocytes, which reduces MMP-1.

References:

1 Lintner K, Peschard O. Biologically active peptides: from a laboratory bench curiosity to a functional skin care product. International Journal of Cosmetic Science 2000;22:207-218.

2 Peptide Sciences.com

3 Dr. Karl Lintner (Ph.D. Biochemist)

4 Leroux R, Lintner K et al. Shaping up. Soap, Perfumery and Cosmetics 2000;73(12):22-24.

5 Katayama K, Armendariz-Borunda J et al. A pentapeptide from type I procollagen promotes extracellular matrix production. J Biol Chem 1993;268(14):9941-4.

6 Katayama K, Seyer JM et al. Regulation of extracellular matrix production by chemically synthesized subfragments of type I collagen carboxy propeptide. Biochemistry 1991;30(29): 7097-104.

7 Harris ED, Rayton JK et al. Copper and the synthesis of elastin and collagen. Ciba Found Symp 1980;79:163-82.

8 Pickart, L; Thaler, MM. Tripeptide in human serum which prolongs survival of normal liver cells and stimulates growth in neoplastic liver. Nature New Biol 1973;243(124):85–87.

9 Pickart L. Use of GHL-Cu as a wound-healing and anti-inflammatory agent. 1988,http://www.freepatentsonline.com/4760051.html.

10 Downey D., Larrabee W. F., Jr., Voci V., Pickart L. Acceleration of wound healing using glycyl-histidyl-lysine copper (II) Surgical Forum 1985;25:573–575.

11 Pickart L. Iamin: a human growth factor with multiple wound-healing properties. In: Sorenson J., editor. Biology of Copper Complexes 1987. Clifton, NJ, USA: Humana Press; 1987. pp. 273–285.

12 Gorouhi, F.; Maibach, H.I. Role of topical peptides in preventing and treating aged skin. Int. J. Cosm. Sci 2009;31:327–345.

13 Burbach JP. What are neuropeptides? Methods Mol Biol. 2011;789:1-36.