

Powerful peptides

Small, biologically active peptides can help slow facial ageing, reduce dark circles under the eyes and lighten unwanted spots, write **Barbara A Green RPh, MS** and **Ronni Weinkauf PhD**

The topical replacement of certain peptides could reinvigorate the natural processes involved in connective tissue renewal and cell proliferation. Although peptides have generally been considered too large for good cutaneous penetration, they can be effectively incorporated into cosmetic care products if they are small enough, stabilised and made sufficiently fat-soluble.

Fibroblast cells ensure the cohesion and good maintenance of dermal connective tissue through production of the protein and glycoprotein components of the extracellular matrix. When incubated with human fibroblasts at concentrations of up to 5 ppm, the peptide Pal-GHK (palmitoyl-glycyl-histidyllysine; palmitoyl oligopeptide) was found to increase de novo glycosaminoglycan synthesis by 46% and collagen synthesis by up to 350%.

The dermal protective and repairing effect of this peptide was evaluated in skin biopsy samples that had undergone UVA irradiation to simulate photoageing. Following treatment with Pal-GHK at a concentration of 5 ppm, these irradiated skin samples exhibited an increase in collagen fibre density compared to pretreatment. The effect of Pal-GHK on skin thickness (epidermis/dermis) was measured in 23 participants following daily application to their forearms. Over four weeks, the topical cream, containing Pal-GHK at a concentration of 4 ppm, produced a significant increase in skin thickness compared with a placebo cream ($P < .05$).

Another structurally related peptide, Pal-GQPR (Palmitoyl-Glycyl-Glutaminyl-Prolyl-Arginine; palmitoyl tetrapeptide-7), has also been shown to improve skin quality. When 17 participants applied a cream formulated with Pal-GQPR at a concentration of 15 ppm for one month, skin firmness increased by 19% and 40% in the face and neck, respectively, and skin elasticity increased by 17% and 27% in the face and neck, respectively. Examination of the skin surface in the same participants revealed enhanced smoothness, a 56% decrease in the deepest wrinkles, and a 14% overall reduction in skin roughness after application of the peptide-containing cream for just 15 days.

Synergistic effects

Peptides may have even more pronounced effects on extracellular matrix reconstitution when used in combination. An *in vitro* study looked at the change in markers of collagen production following exposure to Pal-GHK alone, Pal-GQPR alone, or a combination of the two peptides over 72 hours. Greater increases in all of the markers tested—collagen I, fibronectin, and hyaluronic acid—were observed with the combination of peptides than would be accounted for simply by the sum of their effects.

This observation is supported by *in vivo* data. In a two-month clinical study, 24 female volunteers (aged 42–67 years) applied a commercial preparation containing both Pal-GHK and Pal-GQPR on one side of their faces and a placebo cream containing the vehicle components only on the other side in the morning and again at night. Digital analysis of the crow's feet region after two months found that, whereas the placebo cream had no significant effect, the peptide-containing cream produced smoother skin, a "lifted" surface, and improvement in skin tone.

Pal-GHK and Pal-GQPR are available as Matrixyl 3000 (Sederma SAS, Le Perray en Yvelines, France).

The formation of dark circles and bags under the eyes commonly occurs as a result of erythrocyte leakage from fragile microvessels around the eye. Rupture of these erythrocytes outside of the microvessels releases hemoglobin and, subsequently, its pigmented degradation products—bilirubin/biliverdin and iron. When these products are poorly eliminated, discolouration of the surrounding skin occurs, and over time, this periorbital discoloration can become permanent.

Peptides can reduce the fragility of the skin around the eyes and strengthen the dermal matrix supporting the microvascular network. A recent study looked at the effect on periorbital discoloration of a topical preparation that included the peptides Pal-GHK and Pal-GQPR in combination with the flavenoid chrysin (which enhances elimination of the bilirubin/biliverdin pigments deposited around the eyes) and the chelating agent N-hydroxysuccinimide (which neutralises the cutaneous iron). A group of 22 female volunteers with violet rings under their eyes applied the cream twice daily for eight weeks. Analysis of skin colour using a computerised image processing program demonstrated markedly decreased red pigmentation in 70% of participants and markedly decreased blue pigmentation in 60% of participants.

Pal-GHK and Pal-GQPR are available as Haloxyl (Sederma SAS, Le Perray en Yvelines, France).

Pigmented spots

Oligopeptide-34 has been found to decrease melanin synthesis in skin melanocytes and reduce the transfer of pigment granules, or melanosomes, to keratinocytes. When Asian women with pigmented spots on the skin applied a preparation containing oligopeptide-34 twice daily for eight weeks, a significant lightening effect on those spots was observed using colorimetric measurement. At the end of the eight-week period, 53% of the women rated the results as "good" or "very good", and a further 42% rated the results as "fairly good".

Oligopeptide-34 is available as CG-TGP2 (Caregen Co. Ltd., Gyeonggi-do, Korea).

Barbara A. Green, RPh, MS, is vice-president of clinical affairs and Ronni Weinkauf, PhD, is vice-president of research and development at NeoStrata Company, Inc in Princeton, New Jersey



Caregen Oligopeptide-34: Noticeable lightening of pigmented spots in an Asian woman after application of 20ppm oligopeptide-34 in a cream formulation used twice daily for eight weeks