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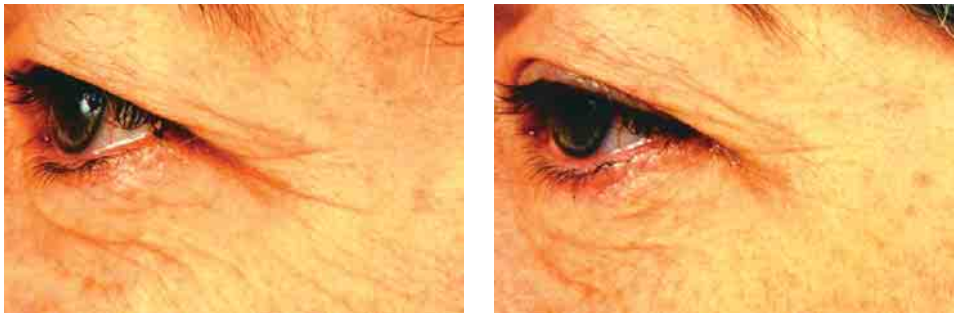
Studies demonstrate value of procollagen fragment Pal-KTTKS

Pal-KTTKS improves wrinkle appearance without causing irritation; shows positive changes in elastin

BY CHERYL GUTTMAN STAFF CORRESPONDENT



Eye zone shown at day one (left) and after four months of treatment with 3 ppm Pal-KTTKS. (Photographs courtesy of Karl Lintner, Ph.D.)

Paris — Results from a series of studies presented at the World Congress of Dermatology support the conclusion that palmitoyl-pentapeptide 3 (Pal-KTTKS) is a very safe and effective agent for improving the appearance of photoaged facial skin.

Pal-KTTKS (Matrixyl) is a modified chain of five amino acids developed as a cosmetic active ingredient and patented, manufactured, and sold for commercial use by the French company Sederma SA. Results of a Sederma-sponsored study demonstrated topical application of a product containing 3 ppm Pal-KTTKS improved wrinkle appearance more quickly than retinol and without causing irritation. The clinical benefits of Pal-KTTKS were confirmed in a separate study that also included histological assessments showing positive changes in elastin and collagen IV.

The efficacy and safety of the modified pentapeptide were also demonstrated in a randomized, double-blind, split-face clinical study undertaken by Procter & Gamble, in which objective and subjective outcome assessments performed after 12 weeks of treatment showed significant benefits of the active formulation for reducing the appearance of fine lines and wrinkles, age spots, and skin firmness. Those improvements occurred with excellent tolerability and without compromising barrier function.

Baseline (left) and 12 weeks after clinical test of product containing 3 ppm Pal-KTTKS. Results in both technically measurable and self-assessed significant improvements in the appearance of fine lines and wrinkles versus placebo. (Photographs courtesy of Donald L. Bissett, Ph.D.)

"Pal-KTTKS has undergone extensive in vitro and in vivo testing, including a wide range of toxicological investigations and with data being reported on more than 200 panelists participating in five independent clinical trials. Based on the evidence accumulated through that research program, I think it is fair to state that this active peptide is a viable alternative to retinoids, in particular retinol, for wrinkle repair. To our knowledge, its high potency, ease of formulation, and the total absence of irritation potential set it apart from any other 'wrinkle treatment active' presently proposed for cosmetic applications," said Karl Lintner, Ph.D., managing and technical director, Sederma SA, Paris.

Down the road

"Pal-KTTKS appears to be very intriguing technology. We are keeping it in our arsenal of active ingredients to consider for future products, and currently we are continuing our formulation work to develop an aesthetically pleasing product for further testing," said Donald L. Bissett, Ph.D., a research fellow in the Skin Care Group, The Procter & Gamble Co., Cincinnati, Ohio.

The Sederma-sponsored histological study was undertaken with the collaboration of Jean Revuz, M.D., professor of der-

matology, Hospital Mondor, France, and president, 20th World Congress of Dermatology. It was a four-month, double-blind study in which 49 women applied Pal-KTTKS (n=22) or vehicle (n=27) twice daily to the face and décolleté. Profilometry and 3D digital image analysis showed sites treated with Pal-KTTKS exhibited significant improvements in skin roughness (-13 percent), wrinkle volume (-36 percent), and wrinkle depth (-27 percent), while there were no changes in any of those endpoints with the vehicle.

Skin biopsies were taken from six women after two and four months, and the results were consistent with the clinical benefits observed. The histological assessments showed Pal-KTTKS application was associated with increases in elastin fiber density and thickness and improved regularity of collagen IV at the dermal-epidermal junction, Dr. Lintner reported.

"Both of these proteins are critical supporting elements in smooth, supple skin," he said.

The active controlled study compared the effects of cosmetic creams containing Pal-KTTKS 3 ppm or retinol 700 ppm on photoaged skin in 16 subjects. It used a split-face, double-blind design and included profilometry, echography, and clinical assessments after two and four months of treatment.

Sans irritation

A benefit of Pal-KTTKS over retinol for reducing wrinkles was noted after two months and that occurred in the absence of irritation reactions. At study conclusion, further improvement in wrinkles and overall roughness was noted in Pal-KTTKS-treated skin along with an average 9 percent increase in skin thickness in Pal-KTTKS-treated skin. At that time, similar changes were noted with retinol treatment.

"DNA array studies show that both Pal-KTTKS and retinol activate genes associated with wound healing mechanisms, but that Pal-KTTKS does not elicit the pro-inflammatory actions associated with retinol," Dr. Lintner said.

"The mechanism studies indicate that KTTKS, like retinoids, improves the appearance of photodamaged skin by stimulating collagen production, however, it seems to do so without causing the irritation that is associated with retinoids. That can be an important benefit in clinical use because a lot of consumers avoid or discontinue topical retinoids because of the side effects," Dr. Bissett said.

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>
> **Karl Lintner, Ph.D.**

Study parameters

The Procter & Gamble study he conducted enrolled 92 women aged 35 to 55 years of age with moderate to severe photodamage and Fitzpatrick skin types I to III. After a two-week preconditioning period, women began applying Pal-KTTKS in a moisturizing base to one side of the face twice daily and the vehicle contralaterally. No other skin care products except for a supplied facial cleanser and a broad spectrum UV sunscreen were allowed.

Changes in fine lines and wrinkles were assessed by comparisons of high-resolution digital images taken at baseline and every four weeks during treatment. Efficacy was assessed both by digital image analysis and trained graders, and the study participants were also asked to rate effects on their skin appearance.

Treatment benefits for improving fine lines and wrinkles were noted as early as four weeks after starting Pal-KTTKS application. At 12 weeks, wrinkle length was reduced from 170.4 mm at baseline to 147.7 mm, and the participants' subjective ratings indicated significant benefits for improving age spots, dark circles, and skin firmness.

The study methods also included measurement of transepidermal water loss at baseline and every four weeks, and those results revealed no negative effects of Pal-KTTKS on the skin barrier, and overall the treatment was very well tolerated, Dr. Bissett reported.

KTTKS, a fragment of alpha-procollagen I, was originally synthesized and investigated at the University of Tennessee based on knowledge that collagen fragments might act through a feedback mechanism to regulate collagen synthesis. Initial studies performed by those investigators in fibroblast cultures showed the pentapeptide increased production of the extracellular matrix proteins collagen I, collagen III, and fibronectin. That activity prompted interest in the potential value of KTTKS as an ingredient in anti-aging skin products.

However, as percutaneous penetration of the water-soluble, charged peptide is poor, scientists at Sederma conjugated KTTKS with palmitoyl, a 16-carbon fatty acid moiety. They confirmed the modified compound diffuses through the stratum corneum and into the skin and showed in vitro and ex vivo that it increases collagen I and glycosaminoglycan synthesis. **DT**