Efficacy and Tolerability of Kinetin 0.1% Cream for Improving the Signs of Photoaging in Facial and Neck Skin

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This study was designed to evaluate the tolerability and efficacy of a moisturizing cream containing kinetin (N^6-furfuryladenine) 0.1% for improving the signs of age-related changes in facial and neck skin.

Eighteen patients (age range, 21–64 years) with mild to moderate photodamage were enrolled in the study. Subjects applied kinetin 0.1% cream combined with sunscreen (sun protection factor 30) twice daily to the face and neck, once in the morning and again in the evening 1 hour before bedtime, for up to 24 weeks. Evaluations included patient assessment of overall skin improvement and improvement in roughness, laxity, mottled hyperpigmentation, fine wrinkles, texture, and blotchiness. VISIA®, a complexion-analysis system, was used to provide an objective measurement of porphyrins, pores, wrinkles, visible spots, and UV spots. Ultrasound (DermaScan™) was used to measure skin collagen density at each visit. Patients were assessed at baseline and at 6, 12, 18, and 24 weeks. Results suggest kinetin 0.1% cream combined with sunscreen may be an effective treatment option for improving skin appearance in people with mild to moderate photodamage without the cutaneous adverse effects associated with other commonly used antiaging products, such as retinoids.

Kinetin (N^6-furfuryladenine) is an essential plant growth factor that regulates various aspects of cellular growth and differentiation. The antiaging actions of kinetin on human skin were first demonstrated by Rattan and Clark[1] in cultured human fibroblasts, where the presence of this cytokinin delayed the onset and decreased the extent of many morphological and biochemical characteristics associated with serial passaging of cells. The effectiveness of kinetin in maintaining normal cell function in aging cells provides the basis for its use in preserving the vitality of aging skin.

Recent studies have shown that kinetin is a powerful antioxidant that helps offset skin aging. Two 52-week studies with a total of 90 subjects were previously conducted to assess the tolerability and effectiveness of topical kinetin for the treatment of mild to moderate photodamaged facial and neck skin.[2] Treatments after 12 and 24 weeks produced significant improvement in the appearance of skin texture, mottled hyperpigmentation, and fine wrinkles compared with baseline as assessed by both the physician and the subject. Treatments also

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produced an improvement in skin barrier function as assessed by a decrease in transepidermal water loss. Our current study expands on these data by incorporating clinical and objective measures of skin improvement. This study evaluates the cosmetic efficacy and tolerability of a moisturizing cream containing kinetin 0.1%.

METHODS AND MATERIALS

The study population was comprised of 18 subjects with mild to moderate photodamage associated with skin aging. Eighteen subjects completed 12 weeks of treatment, and 11 of those subjects elected to continue the treatment through week 24. Inclusion criteria required subjects to be 21 years of age or older and in good health; subjects' ages ranged from 21 to 64 years. Study participants must have had mild to moderate photodamage of facial and neck skin and be willing to refrain from using lotions, moisturizers, cleansers, other skin care products, or any medications on the face and neck other than sunscreen during the treatment period. Subjects with any of the following were excluded: any chronic or recurring skin disease affecting the face or neck; a history of tanning bed use or excessive prolonged exposure to the sun; corticosteroid use within 3 months; retinoid use within 2 months; a history of medium to light trichloroacetic acid peels within 3 months; a history of invasive facial cosmetic procedures, rhytidectomy, blepharoplasty, or facial implants within 12 months; botulinum toxin injections, facial fillers, or nonablative laser rejuvenation, including microdermabrasion, within 6 months; and unwillingness to use sun protection factor (SPF) 30 sunscreen daily during the study. Also excluded were females who were pregnant, nursing, or considering pregnancy.

Subjects applied kinetin 0.1% cream (with SPF 30 sunscreen incorporated) to facial and neck skin twice daily, once in the early morning and once in the evening approximately 1 hour before bedtime, for up to 24 weeks. All 18 subjects completed the study to week 12 and were given the option of continuing the study for an additional 12 weeks. Eleven subjects completed the study to week 24. Recruiting patients for a split-face trial or a placebo arm for our study in a major metropolitan city proved difficult because patients were concerned about having one side of the face look different from the other. Patients also indicated that they would not participate if they might be placed in the placebo group. Therefore, baseline assessments were made as follows, and all evaluations were compared with the baseline assessment.

VISIA®, a complexion-analysis system, was used to provide an objective measurement (±5%–8%) of skin evenness and of the number of porphyrins, pores, wrinkles, visible spots, and UV spots on the skin at baseline and at weeks 6, 12, 18, and 24. Digital photographs were taken at baseline and at weeks 6, 12, 18, and 24. Figure 1 shows subjects before and after 24 weeks of treatment.

DermaScan™, an ultrasound scanning device, was used to determine site-specific collagen density with low-, medium-, and high-density measurements based on specific ultrasound reflection characteristics of the skin. The ultrasound beam penetrates approximately 1.5 mm deep. Depending on the thickness of the dermis being scanned, it will penetrate to either the papillary or the reticular dermis. The scanner, however, does not differentiate papillary from reticular dermis. Ultrasound measurements were made at baseline and at weeks 6, 12, 18, and 24.

A survey was completed by subjects who completed 24 weeks of treatment. Surveys were taken at weeks 12 and 24. They included questions that focused on the patients' perceptions of improvement of their skin quality and their tolerability of the study cream. The surveys assessed skin texture, color, fine wrinkles, blotchiness, and overall improvement. A 6-point grading scale was used to assess each parameter: 6=worse than baseline, 5=no improvement (0%), 4=slight improvement (1%–25%), 3=moderate improvement (26%–50%), 2=marked improvement (51%–75%), 1=excellent improvement (76%–100%).

RESULTS

The average number of UV spots at baseline was 69, which decreased to 43 at week 24 (Figure 2). Fifteen of 18 patients had a reduction of UV spots at week 6; the average reduction was approximately 60%. At weeks 12, 18, and 24, improvements remained constant, but additional reductions were not seen. The mean porphyrin count was 262 at baseline, which decreased to 101 by week 24 (Figure 3). Sixteen of 18 subjects had a reduction of porphyrins at week 6; the average reduction was approximately 80%. At weeks 12, 18, and 24, improvements remained constant, but additional improvements were not seen. Ultrasound scans showed that, of 18 patients, 6 had an increase in low-density collagen at 6 weeks and 11 demonstrated an increase at 12 weeks. At both 18 and 24 weeks, 7 of 11 patients showed a similar increase in low-density collagen (Figure 4). Patient self-assessments at weeks 12 and 24 are shown in the Table. All patients tolerated the study cream well, and no adverse events related to the cream were reported. At 12 weeks, 44% of the study patients reported a moderate to marked improvement in their skin overall. Forty-four percent noted a moderate to marked improvement in skin texture, and 22% reported a moderate to marked improvement in skin color. Twenty-eight percent of patients reported improvement in blotchiness.

At 24 weeks, 55% of subjects noted moderate or greater overall improvement. Seventy-two percent of patients

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Figure not available online

A

Figure not available online

C

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B

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D

Figure 1. Patients at baseline (A, B) and after 24 weeks of treatment with kinetin 0.1% cream (C, D).

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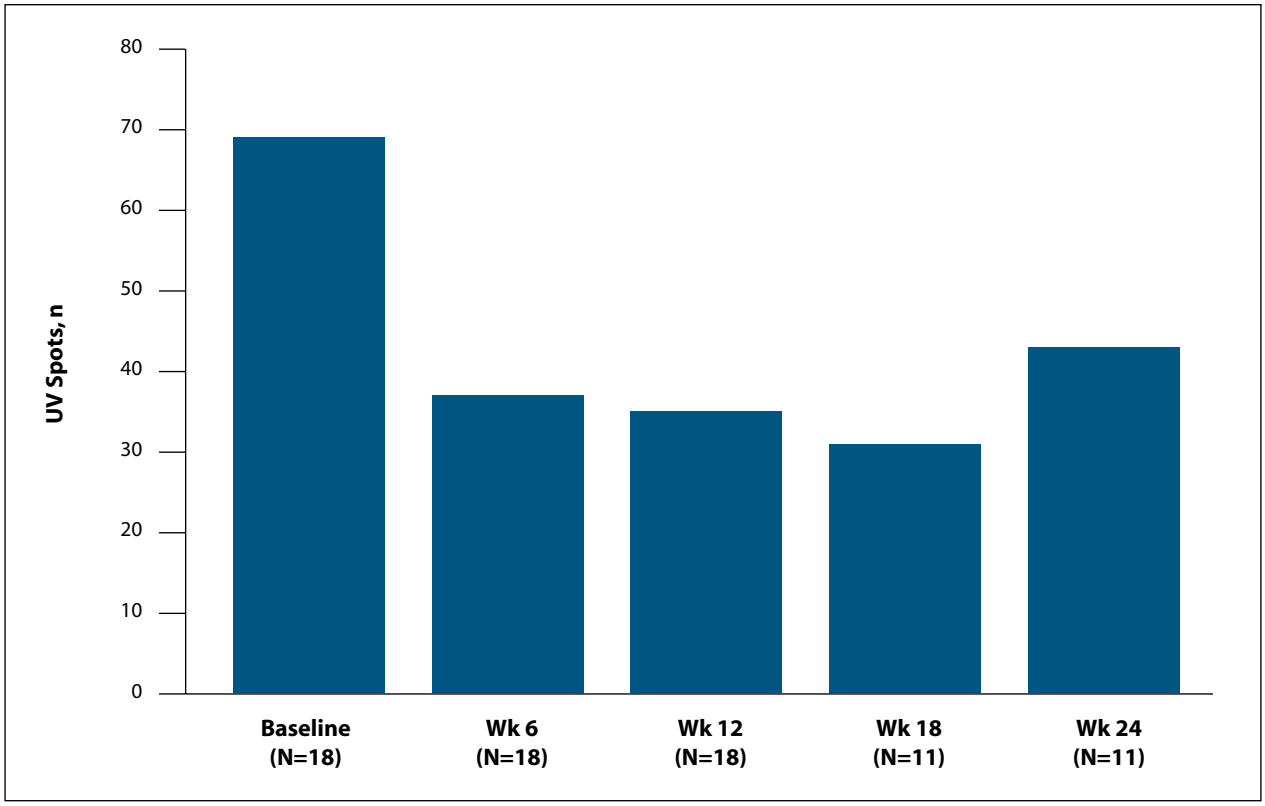

Figure 2. Mean number of UV spots measured n subjects' facial and neck skin during 24 weeks of treatment with kinetin 0.1% cream.

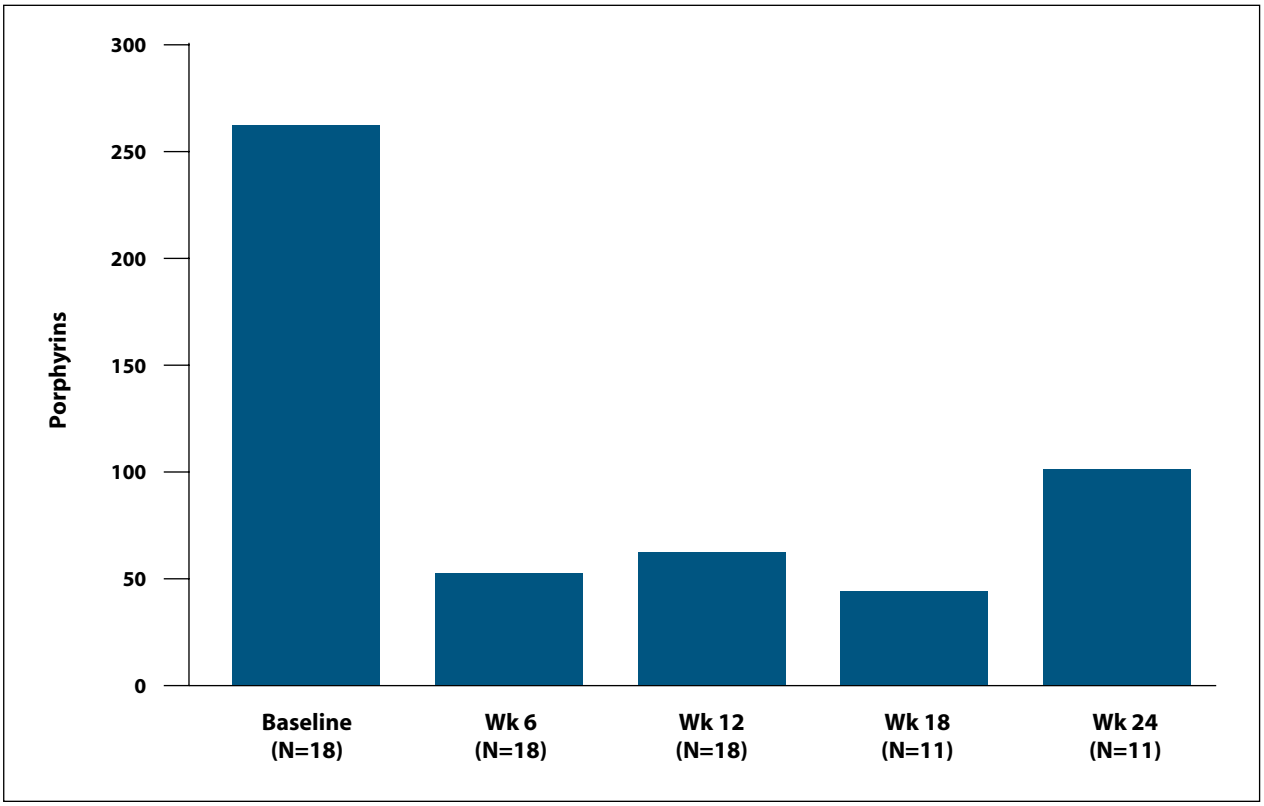

Figure 3. Mean porphyrin count measured on subjects' facial and neck skin during 24 weeks of treatment with kinetin 0.1% cream.

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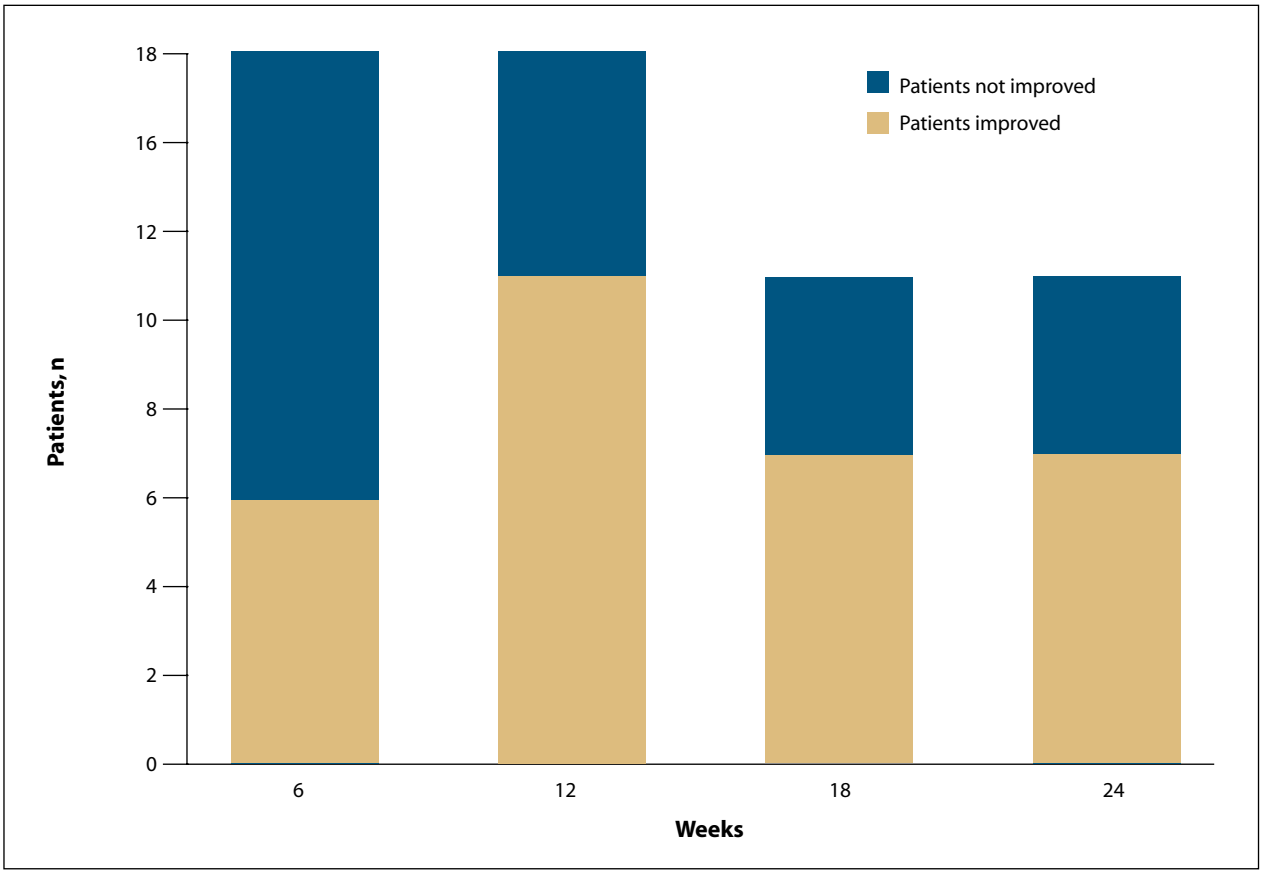

Figure 4. Assessment of low-density collagen in subjects' facial and neck skin during 24 weeks of treatment with kinetin 0.1% cream.

reported an improvement in skin texture and color, and 45% of subjects noted improvement in blotchiness. Nine percent of patients reported a worsening of fine wrinkling, but no subjects reported worsening overall.

DISCUSSION

Kinetin is a plant-derived cytokinin that regulates several aspects of cellular growth and differentiation and is also a powerful antioxidant. Although the effectiveness of kinetin in maintaining normal cell function in aging cells provides the basis for its use in preserving the vitality of aging skin, the exact mechanism of action of kinetin is unknown. This molecule has been introduced into a variety of cosmetic products. The results of our study using kinetin 0.1% cream demonstrate that the majority of patients experienced an improvement in several signs of skin aging in as few as 6 weeks. Patients reported their complexions to be smoother and more even in appearance. Almost all patients experienced a reduction in the number of UV spots and porphyrins as measured by the VISIA complexion-analysis system. Although the mean number of UV spots and porphyrins was lowest at week 18, both were noted to have increased by week 24. This can be attributed to a seasonal increase in sun exposure. With increased ambient temperature, there is also an increase in sebaceous gland activity, resulting in increased *Propionibacterium acnes*, which naturally accumulate porphyrins. Likewise, the initial decrease in both the mean number of UV spots and the mean porphyrin count may correlate with decreased sun exposure and the SPF 30 that was present in the cream. Although porphyrins were measured as an integral component of the VISIA analysis, there is no evidence to suggest that they are implicated in photoaging in facial and neck skin. Because porphyrins are produced by skin bacteria, the reduced number of porphyrins suggests that kinetin might have implications for the treatment of acne. Other parameters analyzed by VISIA did not demonstrate measurable changes of note. It is of particular interest that neither the patients nor the VISIA analysis noted much change in wrinkles. Ultrasound scanning revealed that more than half of the patients had a mild increase in low-density collagen, possibly reflecting the production of new type 1 collagen. Although medium- and high-density collagen were assessed, no change of these measurements from baseline to completion of the study at 24 weeks was noted. This suggests that kinetin may improve deeper UV damage. The cream was very well tolerated, without the cutaneous adverse effects and

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Patient Self-Assessed Improvement Score 12 and 24 Weeks After Beginning Treatment With Kinetin 0.1% Cream

	Improvement, %					
	Excellent	Marked	Moderate	Slight	None	Worse
Skin texture						
12 wk	0	22	22	33	22	0
24 wk	0	36	36	18	9	0
Skin color						
12 wk	0	6	16	22	56	0
24 wk	0	45	27	27	0	0
Blotchiness						
12 wk	0	6	22	16	56	0
24 wk	0	25	18	27	18	0
Fine wrinkles						
12 wk	0	0	11	33	56	0
24 wk	9	0	27	27	27	9
Overall improvement						
12 wk	0	6	38	16	38	0
24 wk	1	9	45	36	9	0

skin irritation often associated with other commonly used antiaging products, such as topical retinoids.

This study suggests that kinetin 0.1% cream is an effective and well-tolerated treatment option for improving the signs and symptoms of photo-induced aging of facial and neck skin.

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