

Clinical Study of Safety and Efficacy of Using Topical Kinetin 0.1% (Kinerase[®]) to Treat Photodamaged Skin

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The purpose of this open-label study was to determine the safety and efficacy of twice-daily application of kinetin (N⁶-furfuryladenine) 0.1% (Kinerase[®], ICN Pharmaceuticals, Costa Mesa, California) lotion for the treatment of mildly to moderately photodamaged facial skin. Treatments lasting 12 and 24 weeks significantly improved the appearance of skin texture, mottled hyperpigmentation, and fine wrinkles as assessed by both physician and patient. Treatments also improved skin-barrier function as measured by a decrease in transepidermal water loss. Overall, these treatments were well tolerated by patients. Kinetin lotion, a new product, is useful in improving the appearance of mildly to moderately photodamaged facial skin and does not produce the cutaneous side effects associated with other commonly used antiaging products.

Kinetin (N⁶-furfuryladenine) is an ingredient in Kinerase[®] (ICN Pharmaceuticals, Costa Mesa, California), a new line of proprietary topical antiaging skin care products. Kinetin is an essential plant growth factor that regulates various aspects of plant growth and differentiation. Kinetin retards senescence in plants (ie, prevents aging of leaves).¹ Rattan and Clark² were the first to show the antiaging effects of kinetin on human skin (in cultured human fibroblasts); kinetin delayed the onset and decreased the extent of many morphologic and biochemical changes associated with serial passaging of cells. The effectiveness of kinetin in maintaining normal cell function in aging cells provides the basis for investigating kinetin as a candidate for preserving the vitality of aging skin.

METHODS

Patients

Enrolled in this single-center, open-label clinical study were 32 patients who were at least 30 years old, in good general health, and who had mildly to moderately photodamaged facial skin. Mean age was 49 years (range, 32–70 years). Thirty (94%) of the patients were women, and 2 (6%) were men. Nine (28%) of the patients had mild photodamage (grade 1 or 2), and 23 (72%) had moderate photodamage (grades 3–6). Patients with severe photodamage (grades 7–9) were excluded from the study. Exclusion criteria included chronic or recurring skin disease or disorder, skin cancer visible on the face, pregnancy, use of Accutane[®] (Roche, Nutley, New Jersey)

within 6 months of study entry, use of topical Retin-A[®] or Renova[®] (Ortho Neutrogena, Los Angeles) within 2 months of study entry, and use of topical α -hydroxy acid skin care products within 1 month of study entry. The protocol was approved by an institutional review board, and informed consent was obtained from all patients.

Treatment Regimen

Patients were instructed to wash their faces and apply the kinetin lotion to the entire face twice daily (morning and evening) for 24 weeks. After completing the 24-week treatment phase, patients were given the option of continuing the treatment for an additional 24 weeks to establish the safety of extended use. All patients used a standardized skin care regimen consisting of application of a mild facial cleanser twice daily, prior to applying Kinetin lotion and daily application of SPF 15 sunscreen beginning 1 week before baseline and continuing for the duration of the study. Patients were in-

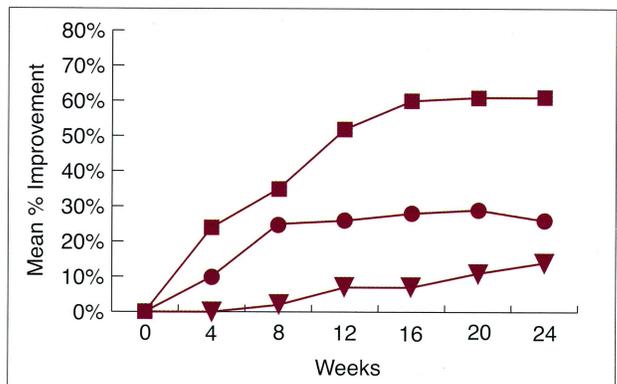


Figure 1. Physician evaluation of clinical signs of photodamage—mean percentage changes in tactile skin roughness ■, mottling ●, and fine wrinkles ▼.

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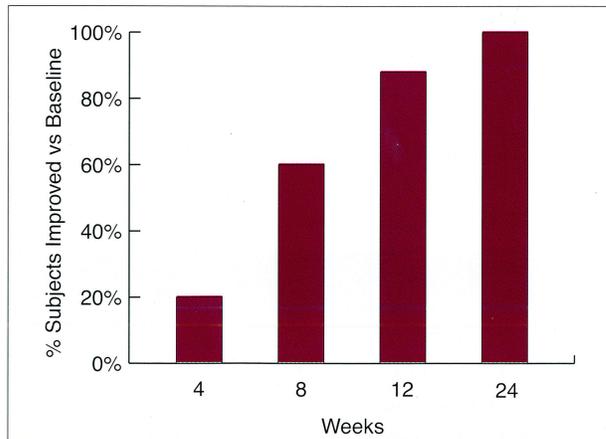


Figure 2. Physician evaluation of global improvement from baseline.

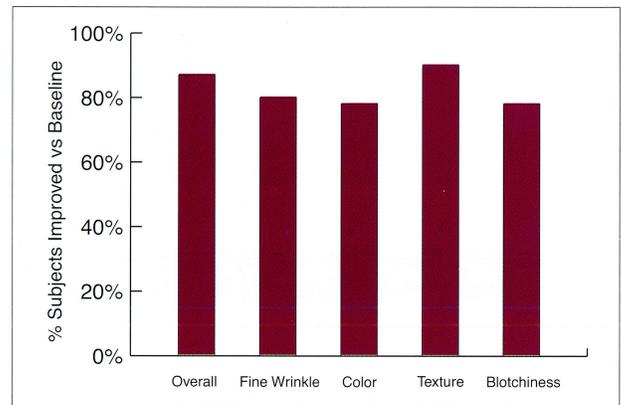


Figure 3. Patient self-assessment results—percentage of patients who reported improvement in individual parameters from baseline to week 24.



Figure 4. Right side of face (A) at baseline and (B) after 12 weeks of treatment. Crow's feet of left side of face of same patient (C) at baseline and (D) after 12 weeks of treatment. Note improvement in skin texture and reduction in fine wrinkling and blotchiness.

structed to continue to use their same brand of makeup during the study and not to wear cosmetics at the time of study evaluation or photography.

Clinical Assessment

Patients were evaluated by the physician at baseline and at monthly intervals for the first 24 weeks for overall severity and clinical signs (roughness, mottling, fine wrinkles) of photodamage using a 10-point scale with points labeled 0 (*none*), 1 to 3 (*mild*), 4 to 6 (*moderate*), and 7 to 9 (*severe*). Global improvement compared with baseline was graded by the physician at each fol-

low-up visit using a 6-point scale with points labeled 0 (*no signs of photodamage*), 1 (*markedly [75%] improved*), 2 (*moderately [50%] improved*), 3 (*slightly [25%] improved*), 4 (*no improvement*), and 5 (*worse*). Using the same scale, patients graded improvement in fine wrinkles, skin texture, and color and overall improvement. For each patient, clinical photographs of the entire face and close-up photographs of the crow's-feet area were taken at baseline and at weeks 12 and 24 using a stereotactic face device provided by Canfield Scientific (Fairfield, New Jersey). The clinical photographs were not used for clinical grading. An evap-

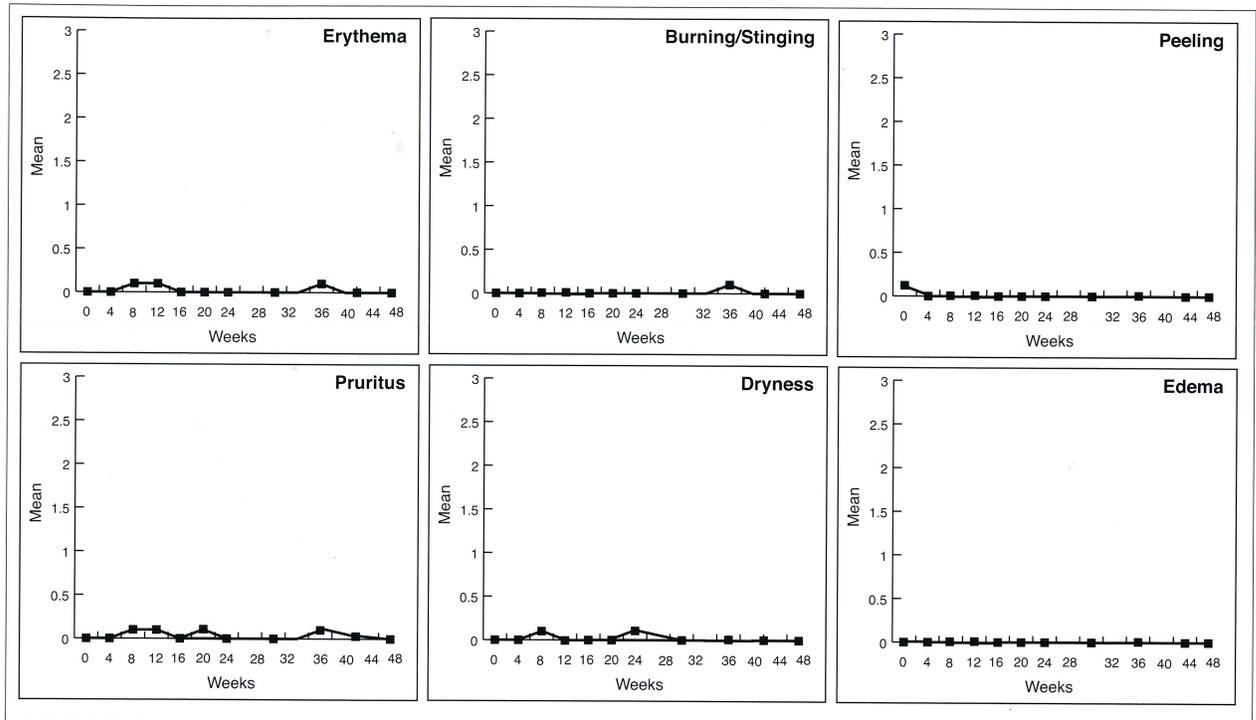


Figure 5. Mean skin irritation score after treatment for as long as 48 weeks. Points on the grading scale were labeled 0 (*none*), 1 (*mild*), 2 (*moderate*), and 3 (*severe*).

orimeter (Servo Med EP2) was used to measure transepidermal water loss (TEWL), an indicator of skin-barrier function.

Safety Assessment

Routine blood and urine chemistry and hematology tests were conducted at baseline and at weeks 24 and 48. The physician assessed the safety of skin irritations and adverse events at each follow-up visit.

Statistical Analysis

Results of treatment vs baseline scores were assessed using paired Student *t*-test and Wilcoxon signed rank test. All statistical tests were 2-sided, and values of .05 or less were considered statistically significant.

RESULTS

Clinical Assessment

Thirty of the 32 patients completed the 6-month efficacy study. Mean overall score for photodamage severity decreased from 4.45 at baseline to 3.93 at week 24—a 12%, statistically significant ($P < .001$) change. All 3 key components of photodamaged skin—tactile skin roughness, mottled hyperpigmentation, and fine wrinkles—showed significant ($P < .001$) improvement from baseline at both 12 and 24 weeks (Figure 1). Tactile skin roughness improved first, with 24% improvement by week 4

and 60% improvement by week 24. Mottling improved 25% by week 12 and 27% by week 24. Fine wrinkles improved gradually after 8 weeks, and improvement averaged 13% by week 24. Physician-assessed global improvement increased steadily, as seen in the percentage of patients improving from baseline, with 100% of patients improving by week 24 (Figure 2). Patient-assessed improvement in photodamage was consistently higher than physician-assessed improvement. At week 24, 87% of patients reported overall improvement; 90%, improvement in skin texture; 80%, improvement in fine wrinkles; and 77%, improvement in both skin color and blotchiness (Figure 3). At week 24, 50% of patients graded overall improvement as moderate (50% or more improvement); also, 53% and 40% of patients graded improvement in skin texture and fine wrinkles, respectively, as moderate. The most clinical improvement occurred in the crow's-feet area; skin texture softened, and fine wrinkles and mottling decreased (Figure 4).

TEWL tends to be higher in photodamaged skin—a reflection of an abnormal stratum corneum.³ After 24 weeks, TEWL decreased 26%—an indication of improvement in skin barrier function.

Safety Assessment

Treatments used in this study were well tolerated by most patients. None of the usual signs or symptoms of irritation occurred (Figure 5). Nine patients reported mild

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transient acne as an adverse effect during the initial course of treatment. Most patients continued treatment for the entire 48-week study. After week 12, no one reported any episodes of acne. Two patients discontinued at weeks 8 and 12 because of facial rash and acne, respectively. The routine blood and urine chemistry and hematology tests showed no pathologic changes.

DISCUSSION

Our study showed that topical kinetin 0.1% lotion can partially improve some of the clinical signs of mildly to moderately photodamaged facial skin and can help restore normal skin barrier function after 12 to 24 weeks of application. The mechanism by which kinetin improves the clinical features of photoaging requires further study. Recent studies have shown that kinetin is a powerful antioxidant⁴ that may help protect the skin from free radical damage caused by ultraviolet radiation. In addition to having moisturizing benefits, the ingredients of the vehicle may play an important role in kinetin delivery. As in other studies, a product for treating photodamaged skin, a standardized skin care regimen, and a sunscreen may all have contributed to improving the appearance of some patients. In contrast to the propensity of other antiaging products (retinoids, α -hydroxy acids) to cause irritation,^{5,6} kinetin lotions did not produce clinical signs or subjective symptoms of irritation. Improvement in appearance of photodamaged skin after 12 to 24 weeks of treatment, cosmetic elegance of the formulation, and lack of irritation all contributed to our patients' high level of acceptance of this new antiaging product.

The authors have no financial interest in the products or companies mentioned in the article.

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