Comparative Clinical Efficacy of Three Novel Polyhydroxy Alpha-Hydroxyacids Using Instrumental Assessment

Barbara Green, R.Ph., M.S.[a] **Richard Wildnauer, Ph.D.**[a] **Denise Milligan, B.S.**[b] **Gary Grove, Ph.D.**[b]

[a] NeoStrata Company, Inc., Princeton, NJ

[b] Skin Study Center, Broomall, PA

Introduction

The established benefits of using alpha hydroxyacids (AHAs) in a regular skin care regimen have been determined using a limited selection of common AHAs, with the perception that all AHAs perform similarly. However, numerous different AHAs are available to formulators of topical products increasing the complexity of AHA skin care. Most notably, a second generation of AHAs known as poly-hydroxy AHAs (PHAs), may offer unique characteristics and benefits to skin.

The purpose of this study was to evaluate the clinical efficacy of three novel polyhydroxy AHA compounds utilizing a short but comprehensive in vivo test method, and to determine whether compound specific effects on skin hydration, barrier function and surface topography are observed.

Objectives

1. To evaluate the clinical effects of three novel poly-hydroxy AHA (PHA) compounds in comparison to an untreated control with regard to:
   - Hydration
   - Barrier Function
   - Surface Topography
   - Skin Tolerance
2. To evaluate the testing methodology to determine its suitability for use in differentiating cutaneous effects of various skin care compounds.

Method

- Double-blind, randomized, complete block (n=30) and direct comparison (3 groups n=10), untreated control (UT), 3 week study.
- 30 healthy women (age 40±15) with a history of xerosis were enrolled; 3 subjects withdrew due to reasons unrelated to the study.
- **Test Formulations** included 3 different poly-hydroxy AHAs (PHAs) coded N5, N6, N7 prepared in a cream base at 8%:

Code	# carbons/ molecule	# hydroxyls/ molecule	Form	pH
N5	5	3	Lactone	3.4
N6	6	4	Lactone	3.0
N7	7	4	Acid	3.7

- **Complete block:** 4 test sites (5X5cm) were defined on the volar forearms. 3 different PHAs (8% cream) were tested in comparison to UT. Creams were applied twice daily for 3 weeks using syringes at 2mg/cm².
- **Direct comparison:** Subjects were further divided into 3 subgroups. Each group of 10 subjects was randomly assigned to apply one PHA cream to one lower leg and one side of the face twice daily; the contralateral side served as an untreated control.
- **Clinical evaluations** occurred at baseline and weeks 1, 2 and 3 to ensure compliance and to monitor tolerance to study products.
- **Instrumental assessments** included:
  - **Conductance** (IBS Skicon-200 Conduct-ance Meter) to measure surface hydration on the forearms and legs.
  - **Sorption-Desorption** (IBS Skicon-200) measurements to assess water holding capacity (WHC) on the forearms.
  - **Transepidermal water loss** (TEWL) (Servo Med Evaporimeter) to measure barrier function on the forearms.
  - **D-Squame** samples to examine exfoliation patterns on the legs.
  - **Silicone replicas** with optical profilometry to assess surface topography in the crow's feet region.
- **Statistical analysis** for forearm treatment comparisons was done using Repeated Measures ANOVA; subgroup comparisons were made using Tukey's Protected T-Test. Leg and face data were analyzed using a paired t-test to examine significant differences between each treatment and its respective untreated control.

Results

TEWL

Forearm TEWL values for N5 treated sites were *lower* at endpoint compared to N6, N7, UT ($p<0.01$). N6, N7 were not statistically different from UT. *Barrier Integrity is maintained with PHA use.*

Hydration

- Forearm hydration values were increased for N5 sites compared to N6, N7, UT ($p<0.01$); N7 hydration scores were lower than N6, UT ($p<0.01$).
- Leg hydration scores were greater for each PHA treatment compared to UT; N5 ($p<0.001$), N6 ($p<0.05$), N7 ($p<0.05$).

Sorption-Desorption

Water Holding Capacity was significantly *improved* for N5 compared to N6, N7, UT ($p<0.05$). N6 was improved over N7, UT at endpoint ($p<0.01$).

D-Squame

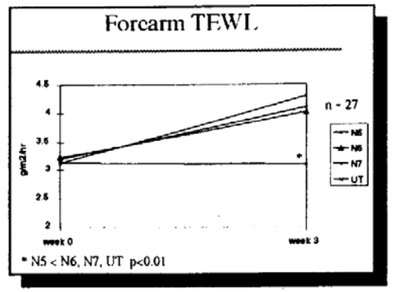
Percent coverage was *lower* for N5 ($p<0.01$) and N7 ($p<0.05$) compared to UT at endpoint.

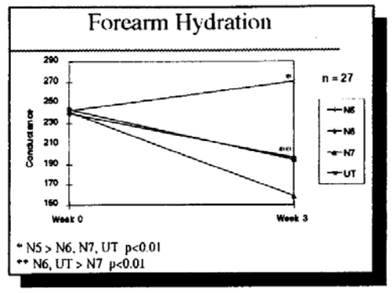
Silicone Replicas

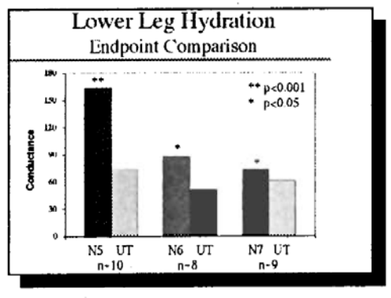
Optical profilometry revealed smoother N7 sites compared to UT ($p<0.05$) and directional improvements for N5, N6 versus UT.

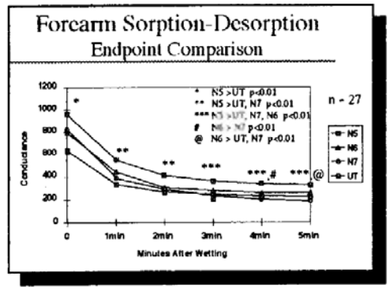
Product Tolerance

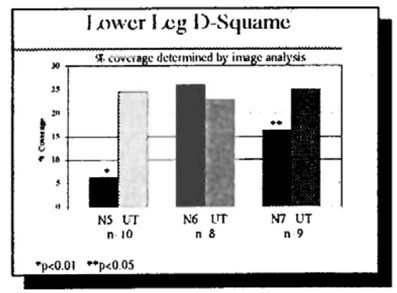
Transient, mild irritation was reported by one subject. There were no discontinuations due to irritation or discomfort.

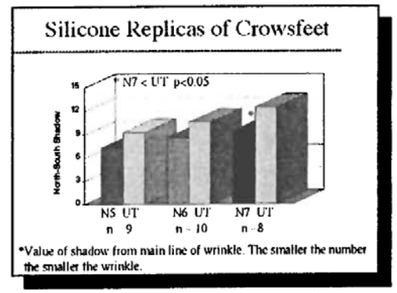












Conclusions

- The test methodology is useful in differentiating clinical benefits of various skin care agents to guide product development.
- The three novel PHA formulations provide measurable skin benefits while maintaining barrier integrity and safety.
- Structurally dissimilar PHA compounds offer different benefits to the skin. N5 was superior to N6, N7 in providing skin conditioning benefits including increased hydration, WHC and maintenance of barrier function.
- Skin hydration may not directly correlate to improvements in surface topography. N7 was effective in improving flaking and wrinkling patterns but was less effective at improving hydration and barrier function.
- Additional studies are required to further investigate structure-activity relationships.