Polyhydroxy Acids (PHAs) Provide Conditioning Effects to Skin Without Increasing Sensitivity to UV Light

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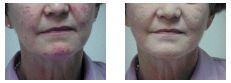
Introduction

The polyhydroxy acids (PHAs) are skin care ingredients that provide additional benefits to skin compared to traditional alpha hydroxyacids (AHAs) such as glycolic acid and lactic acid. Similar to AHAs, PHAs provide exfoliation, skin smoothing and anti-aging effects[1-3]PHAs are also humectants and moisturizers, and most PHAs possess antioxidant properties[4]. [5]In comparison to commonly used AHAs, PHAs do not cause sensory irritation responses that can limit the use of classical AHAs.[2,4]Moreover, PHAs are compatible with clinically sensitive skin including rosacea and atopic dermatitis[2] and corrective cosmetics containing PHAs can be used to conceal skin color irregularities on sensitive skin, e.g. post-laser purpura (FIGURE 1), and haemangiomas as in Sturge-Weber Syndrome[6] PHAs have also been shown to enhance stratum corneum barrier function, increasing the skin's resistance to chemical challenge[7]

New study results indicate that use of PHAs does not result in an increase in sunburn cells in skin following UVB exposure. Therefore, PHAs are an important alternative to AHAs for individuals not able to use sunscreen protection with their AHAs on a daily basis. In addition, PHAs are shown to be compatible with tretinoin use. Combination use of PHAs plus tretinoin may be preferable to glycolic acid plus tretinoin in view of the potential increase in sun sensitivity by tretinoin.

Condition: Skin Discoloration



Post-laser purpura concealed with PHA containing corrective cosmetic

Objective

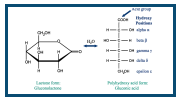
The purpose of this poster is to describe recent study results regarding the benefits of PHAs as they specifically relate to:

- Lack of sunburn cell formation
- Compatibility with topical tretinoin

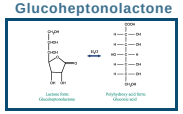
PART I: THE EFFECT OF TOPICAL TREATMENTS ON THE SENSITIVITY OF HUMAN SKIN TO SOLAR SIMULATED RADIATION[x]

The Cosmetics, Toiletries and Fragrances Association (CTFA) and Food and Drug Administration (FDA) have investigated the effects of AHA product usage on the sensitivity of normal human skin to UVB exposure by measuring changes in minimal erythemal doses (MEDs) and numbers of sunburn cells (SBCs). Findings among the studies indicate that there is a significant increase in the sensitivity of skin to UVB after AHA (glycolic acid, 10%) use[8,9], this effect subsides within seven days of discontinuing AHA use.[8] The present two studies were conducted to evaluate the effects of polyhydroxy acids (gluconolactone and glucoheptonolactone) on skin sensitivity to UVB using the model employed by CTFA and FDA.

Gluconolactone



Glucoheptonolactone



Method

- Two separate studies utilizing a complete block design. Products were blinded and randomly assigned to the test sites.
- **Population:** Healthy males and females, Fitzpatrick skin types I, II, and III.
  - Study I: n=10, ages 19-21 years
  - Study II: n=11, ages 20-51 years

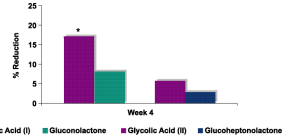
- **Test Materials** (study I)
  - AHA: 8% glycolic acid cream, pH 4.1
  - PHA: 8% gluconolactone cream, pH 4.2
  - Untreated control
- **Test Materials** (study II)
  - AHA: 8% glycolic acid cream, pH 3.8
  - PHA: 8% glucoheptonolactone cream, pH 3.8
  - Untreated control

- **Test Material Application:**
  - Once daily application to marked test sites on the back by study personnel using a 1c.c. disposable plastic tuberculin syringe at a dose of 2mg/cm [2]. Products were thoroughly rubbed into the test sites using a finger cot.
  - Products were applied 6 days per week for 4 weeks.
- **Endpoint MEDs:**
  - Determined at each test site 20±4 hours after exposure to a solar simulator. Test sites were graded visually for erythema under standardized lighting conditions.
- **SunburnCells** (SBCs):
  - Induced by one exposure to 1.5x MED approximately 15 minutes following the last topical application of the test product.
  - Shave biopsies (4x4mm) were obtained 20±4 hours following irradiation. The skin specimens were immediately fixed in 10% buffered formalin.
  - Fixed specimens were processed routinely, paraffin embedded and then sectioned and stained with hematoxylin-eosin.
  - Numbers of SBCs were counted in a blinded manner by the investigator in at least 12 sections at 50 micron intervals. A minimum of 70 high power fields (HPF) was counted from each biopsy and the average number of SBCs per HPF determined.

Results – MEDs

Test Product	MED	Statistical Significance Compared to Untreated
Glycolic acid (Study I)	23.7	p<0.01
Gluconolactone	26.9	Not significant
Untreated	31.1	
Glycolic acid (Study II)	12.6	Not significant
Glucoheptonolactone	13.0	Not significant
Untreated	13.5	

Mean % Reduction in MED Compared to Untreated



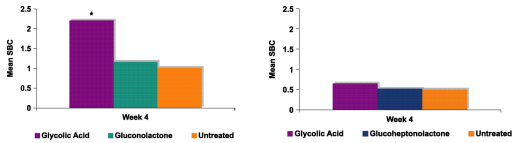
N(I)=10; N(II)=11
* Significant reduction in MED compared to untreated control, p<0.01

- **Conclusions**
  - MEDs appear to be affected by topical product application.
  - Glycolic acid application significantly reduced the MED in study (I), and caused a directional but not statistically significant reduction in MED in study (II) compared to untreated.
  - PHAs (gluconolactone and glucoheptonolactone) did not significantly change the MED compared to untreated.
- **Comment**
  - There is inherent variability in MEDs within a person. Therefore small changes in the MED value may not be clinically relevant.[9]

Results – SBCs

Test Product	SBC/HPF	Statistical Significance Compared to Untreated
Glycolic acid (Study I)	2.21	p<0.05
Gluconolactone	1.16	Not significant
Untreated	1.02	
Glycolic acid (Study II)	0.65	Not significant
Glucoheptonolactone	0.52	Not significant
Untreated	0.50	

Mean Sunburn Cell Count SBC/HPF



Study I, N=10
*Significant increase in SBCs compared to untreated, p<0.05

Study II, N=11
No significant differences among treatments, p<0.05

- **Conclusions**
  - Glycolic acid caused a significant increase in SBC count in study (I) and a small, directional increase in SBCs in study (II) compared to Untreated.
  - The PHAs (gluconolactone and glucoheptonolactone) did not significantly increase SBCs compared to untreated.
- **Comment**
  - These findings are consistent with previous studies conducted by CTFA and FDA.[8,9,11]However, there was a disparity in values for the two control cells (glycolic acid and untreated) between the two studies demonstrating variability with this model, possibly related to the difference in age groups of the participants between the two studies.

PART II: COMPATIBILITY OF A PHA REGIMEN WITH TOPICAL RETINOIC ACID[y]

Method

PHAs are used adjunctively with topical drug therapies for the treatment of inflammatory skin conditions including psoriasis, rosacea, acne, and seborrheic dermatitis; and various hyperkeratotic condtions including xerosis and keratosis pilaris, as well as fungal infections, hyperpigmentation, and pre- and post-treatment for laser resurfacing[12,13].

The following study was conducted to determine the compatibility of a PHA regimen with topical tretinoin in the treatment of mild to moderate facial acne.

- **Population:**
  - 27 healthy males and females, ages 19-54 years
  - Subjects exhibited mild to moderate facial acne
  - Exclusion for use of: (i) any acne therapy (including topical OTCs or Rx, or systemic medications) one month prior to study, (ii) PHA or AHA products 4 weeks prior to study, or (iii) topical retinoids within 3 months or oral retinoids within 6 months of study initiation
- **Study Design:** Four week normal use regimen with comparisons to baseline
- **Test Materials:** Products were applied to the entire face in a normal use manner as indicated in the table. The PHA products were provided in blinded packaging.

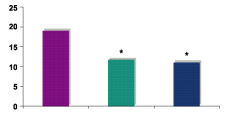
Product	Daily Usage	% PHA (gluconolactone)	pH
Cleanser	AM and PM	4	3.5
Day Lotion SPF 15	AM	4	3.9
0.1% Tretinoin Gel	PM	–	–
Night Cream	PM (after application of tretinoin gel)	15	3.3

- **Assessments**
  - **Clinical assessment** of efficacy included **acne lesion counts** conducted by a board certified dermatologist. Scores were reported as total lesion counts: papules + pustules + open comedones + closed comedones.
  - **Clinical assessments** of irritation were conducted by a board certified dermatologist and included: **objective irritation** (dryness and erythema), and inquiries about **subjective irritation** (itching, burning, stinging, tightness) using a 5 point scale (none, barely perceptible, mild, moderate, severe).
  - **Self assessment** questionnaires were completed to assess consumer perception of efficacy and product tolerability.

Results

- All dermatological parameters remained within normal limits throughout the study.
- **Clinical Assessment - Acne Lesion Counts**
  - Total lesion counts (including papules, pustules, open and closed comedones) significantly decreased throughout the study, thus demonstrating efficacy of the tretinoin formulation in combination with a PHA regimen.

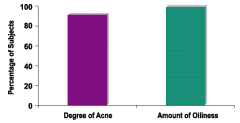
Total Acne Lesion Counts
Tretinoin + PHA Regimen



N=27
*Significant improvements from baseline at Weeks 2 and 4, p<0.05

- **Clinical Assessment - Objective and Subjective Irritation**
  - Mean scores for both objective (dryness and erythema) and subjective (itching, burning, stinging, and tightness) irritation remained less than "barely perceptible" on the 5 point grading scale after 4 weeks of product use.
- **Self Assessment**
  - Self assessment for improvement of acne and oiliness correlated with dermatological lesion count assessments demonstrating product efficacy.

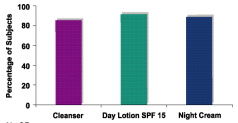
Self Assessment – Improvement of Condition
Tretinoin + PHA Regimen



N=27

  - Over 85% of the subjects reported that the cleanser, day lotion SPF 15, and night cream were compatible with their use of topical tretinoin.

Self Assessment
Compatibility of PHA Products with Tretinoin



N=27

- **Conclusions**
  - The PHA regimen was well tolerated on facial adult acne when combined with tretinoin 0.1% gel.
  - Use of the PHA regimen did not adversely affect tretinoin efficacy in treating acne.
- **Comment**
  - This study supports the use of PHAs in combination with tretinoin for adult acne.

Summary

The polyhydroxy acids (PHAs) have gained important clinical uses as a result of their providing AHA benefits to skin, with additional gentleness and antioxidant characteristics resulting from the polyhydroxy molecule. PHAs are commonly used adjunctively with other topical therapeutic regimens in the treatment of skin disorders[2,13]. The above study indicates that tretinoin 0.1% gel is both well tolerated and effective in the treatment of acne when combined with a PHA regimen.

The Cosmetic Ingredient Review panel suggests use of AHAs (i.e., glycolic acid and lactic acid) in consumer products at a maximum concentration of 10%, and minimum pH of 3.5 when the products are formulated to avoid increasing the skin's sensitivity to sun, or when directions for use on packaging include the daily use of sun protection[9]. Research has shown that low level sunscreens in AHA formulations can prevent the development of SBCs after UV exposure.[15]Nonetheless, some individuals are sensitive to sunscreens and do not apply them on a daily basis. The above studies indicate that application of PHAs (gluconolactone and glucoheptonolactone) does not increase the sensitivity of skin to UVB, and therefore may provide an important formulation option to AHAs, especially for those individuals that are sensitive to sunscreens. In addition, topical PHAs provide a safe and well-tolerated option for combination use with retinoids, which are known to cause photosensitizing effects.

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[1]Study conducted by KGL, Inc. (Ivy Laboratories), Philadelphia, PA
[2]Study conducted by Consumer Product Testing Company, Inc., Fairfield, NJ

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