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A Comparison of the Effectiveness of Topical AC-11 Plus Sunscreen and Sunscreen Alone in Protecting Volunteers From Sunlight-Induced Erythema

Summary

Introduction

Two separate studies have demonstrated significant decreases in cyclobutyl pyrimidine dimers (TT-dimers) when AC-11 was applied topically to human living skin equivalents exposed to UV-B radiation (Mammone et al, 2004; Wachs, 2004). As DNA is the likely chromophore for erythema, it follows that the inhibition of dimers would be reflected in reduced erythema (Young et al, 1998). This study is an initial attempt to characterize the effect of AC-11 on sunlight-induced erythema.

Methods

Forty-two volunteers <mean age?> <male:female ratio?> <ethnicity?> applied two different topical products prior to sun exposure. One of the products was applied to the right side and the other to the left side of their bodies. The two products were <0.5%?> AC-11 plus an SPF 15 <chemical?> sunscreen and the SPF 15 sunscreen only. The products were marked with a code and were otherwise indistinguishable. The investigators assigned which product the volunteers applied to each side. The volunteers were unaware which product contained AC-11 and thus which side was treated with topical AC-11. After sun exposure, volunteers were asked to evaluate the response to the different topical formulations with respect to erythema, blistering, and pain.

Results

The frequency of erythema in AC-11 plus sunscreen-treated sites (6 of 42), was significantly ($p < 0.0001$) reduced compared with sites that were treated with sunscreen only (33 of 42; Figure 1). A similar significant ($p < 0.0001$) reduction was noted in the incidence of blistering (4 of 42 AC-11 plus sunscreen-treated sites and 33 of 42 sunscreen only-treated sites). Pain was reported by 2 of 21 volunteers on the sunscreen-only site and by none on the AC-11 plus sunscreen sites (not significant).

Discussion

DNA is an epidermal chromophore (Young, 1997) which is a likely factor in UV-induced acute epidermal inflammation, such as erythema and sunburn (Ley, 1985). A comparison of the UV spectra that result in epidermal dimer formation and erythema suggest that DNA is a chromophore for erythema at 280-340 nm. Thus, dimer formation and erythema are apparently interrelated phenomena and erythema may serve as indicator of photochemical DNA damage (Sutherland et al, 2002).

Although limited in scope and deficient in controls, this pilot study clearly demonstrated that AC-11, which has been shown to reduce dimers, substantially decreased erythema. It also supports the contention that dimerization is interrelated with erythema, although this study did not measure cyclobutyl pyrimidine dimers.

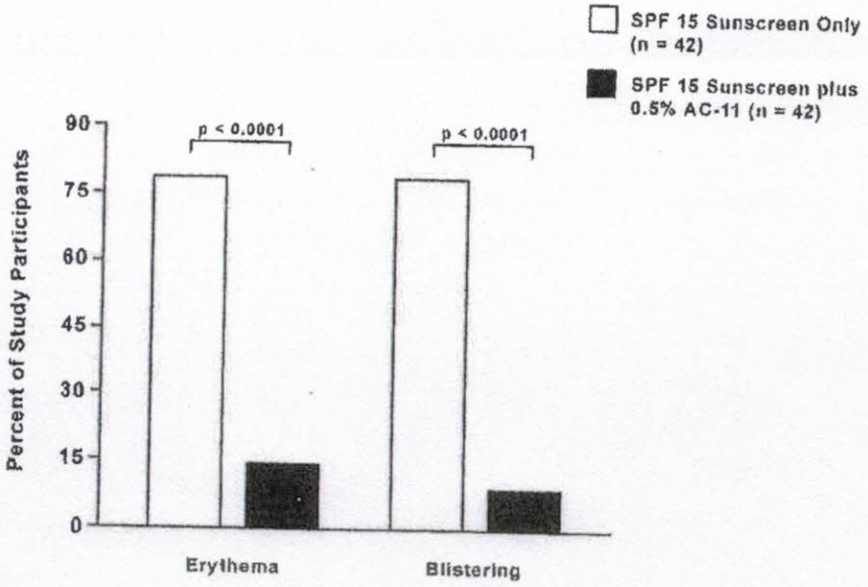

Figure 1. The percent of study participants who noted erythema and blistering on sites where sunscreen only and AC-11 plus sunscreen formulations were applied prior to sun exposure.

References

Ley RD: Photoreactivation of UV-induced pyrimidine dimers and erythema in the marsupial *Monodelphis domestica*. *Proceedings of the National Academy of Sciences USA* 1985;82:2409-2411.

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Sutherland BM, Hacham H, Bennett P, Sutherland JC, Moran M, Gange RW: Repair of cyclobutyl pyrimidine dimers in human skin: variability among normal humans in nucleotide excision and in photorepair. *Photodermatology, Photoimmunology & Photomedicine* 2002;18:109-116.

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Young AR: Chromophores in human skin. *Physics in Medicine and Biology* 1997;42:789-802.

Young AR, Chadwick CA, Harrison GI, Nikaido O, Ramsden J, Potten CS: The similarity of action spectra for thymine dimers in human epidermis and erythema suggests that DNA is the chromophore for erythema. *Journal of Investigative Dermatology* 1998;111:982-988

Sunburn Study; Statistical Analysis; All Data

Erythema

Two-Sample Z-Test (Differences Between Proportions)

Sample One: Vehicle Only
Sample Two: AC11 + Vehicle

Outcome: 1 = Erythema; 0 = No Erythema Present

	Sample 1	Sample 2
Sample Proportion	0.7857*	0.1429†
Sample Size (n)	42.0000	42.0000

z statistic = 5.906
p value (two-tailed) < 0.0001‡

* 33 of 42 with erythema.
† 6 of 42 with erythema.
‡ Fixed output in decimal places.

Based on a benchmark of .05 alpha, the estimated p-value of < 0.0001 suggests there is a statistically significant difference between the two independent sample means.

NOTE, HOWEVER,

	Sunburn Lotion Only	AC11 Plus Sunburn Lotion
N of cases (n)	42	42
Minimum	0.000000000	0.000000000
Maximum	1.000000000	1.000000000
Range	1.000000000	1.000000000
Sum	3.30000E+01	6.000000000
Median	1.000000000	0.000000000
Mean	0.785714286	0.142857143
95% CI Upper	0.915130788	0.253223907
95% CI Lower	0.656297784	0.032490379
Std. Error	0.064082140	0.054649433
Standard Dev	0.415299732	0.354168802
Variance	0.172473868	0.125435540
C.V.	0.528563296	2.479181612
Skewness(G1)	-1.444739675	2.117634293
SE Skewness	0.365360606	0.365360606
Kurtosis(G2)	0.089199689	2.606303419
SE Kurtosis	0.716632727	0.716632727
SW Statistic	**0.505964692**	**0.417281717**
SW P-Value*	**0.000000000**	**0.000000000**

SW = Shapiro-Wilk Normality Test

Chi-square test of Independence

	AC-11*	SLO†
Erythema	6	33
None	36	9

* AC11 = Vehicle (suntan lotion) plus AC-11.
† SLO = Suntan lotion only.

Chi square	df	p <	Cases (n)
34.8920	1	0.0000	84

Test statistic	Value	df	Probability
Pearson Chi-square	3.48923E+01	1.0	0.000000003
Yates corrected Chi-square	**3.23556E+01**	**1.0**	**0.000000013**
Fisher exact test (two-tail)			0.000000004

Kruskal-Wallis One-Way Analysis of Variance for 84 cases

Categorical values encountered during processing are:
THERAPY$ (2 levels)
AC11 (Vehicle [suntan lotion] plus AC-11) and **SLO** (Suntan lotion only)

Dependent variable is ERYTHEMA (0 = none; 1 = erythema observed)
Grouping variable is THERAPY$ (SLO = Suntan Lotion Only; AC11 = Suntan Lotion plus AC-11

Group	Count	Rank Sum
AC11	42	1.21800E+03
SLO	42	2.35200E+03

Mann-Whitney U test statistic = 3.15000E+02
Probability is 0.000000004
Chi-square approximation = 3.44769E+01 with 1 df

Sunburn Study; Statistical Analysis; All Data

Sunburn

Frequencies
THERAPY$ (rows) by SUNBURN (columns)
Outcome: 1 = Sunburn; 0 = No Sunburn Present

	0	1	Total
AC11*	37	5	42
SLO†	10	32	42
Total	47	37	84

* AC11 = Vehicle (suntan lotion) plus AC-11.
† SLO = Suntan lotion only.

Test statistic	Value	df	Probability
Pearson Chi-square	3.52133E+01	1	0.000000003
Yates corrected Chi-square	**3.26532E+01**	**1**	**0.000000011**
Fisher exact test (two-tail)			0.000000003

Kruskal-Wallis One-Way Analysis of Variance for 84 cases

Categorical values encountered during processing are:
THERAPY$ (2 levels)
AC11 (Vehicle [suntan lotion] plus AC-11) and **SLO** (Suntan lotion only)

Dependent variable is SUNBURN (0 = none; 1 = sunburn observed)
Grouping variable is THERAPY$ (SLO = Suntan Lotion Only; AC11 = Suntan Lotion plus AC-11

Dependent variable is SUNBURN
Grouping variable is THERAPY$

Group	Count	Rank Sum
AC11	42	1.21800E+03
SLO	42	2.35200E+03

Mann-Whitney U test statistic = 3.15000E+02
Probability is 0.000000004
Chi-square approximation = 3.47941E+01 with 1 df

Sunburn Study; Statistical Analysis; All Data

Blistering

Frequencies
THERAPY$ (rows) by BLISTERING (columns)
Outcome: 1 = Blistering; 0 = No Blistering Present

	0	1	Total
AC11	38	4	42
SLO	9	33	42
Total	47	37	84

* AC11 = Vehicle (suntan lotion) plus AC-11.
† SLO = Suntan lotion only.

Test statistic	Value	df	Probability
Pearson Chi-square	4.06233E+01	1	0.000000000
Yates corrected Chi-square	**3.78700E+01**	**1**	**0.000000001**
Fisher exact test (two-tail)			0.000000000

Kruskal-Wallis One-Way Analysis of Variance for 84 cases

Categorical values encountered during processing are:
THERAPY$ (2 levels)
AC11 (Vehicle [suntan lotion] plus AC-11) and **SLO** (Suntan lotion only)

Dependent variable is SUNBURN (0 = none; 1 = sunburn observed)
Grouping variable is THERAPY$ (SLO = Suntan Lotion Only; AC11 = Suntan Lotion plus AC-11)

Dependent variable is BLSTERNG
Grouping variable is THERAPY$

Group	Count	Rank Sum
AC11	42	1.17600E+03
SLO	42	2.39400E+03

Mann-Whitney U test statistic = 2.73000E+02
Probability is 0.000000000
Chi-square approximation = 4.01397E+01 with 1 df

Sunburn Study; Statistical Analysis; All Available Data (n = 21)

Pain

Chi-square test of Independence

	AC-11*	SLO†
Pain	0	2
No Pain	21	19

* AC11 = Vehicle (suntan lotion) plus AC-11.
† SLO = Suntan lotion only.

Chi square	df	p <	Cases (n)
2.1000	1	0.1470	42

Warning! Chi-square assumption violated.

Skin Types and Related Conditions

What are the four major skin textures and their characteristics?

1. **Oily Skin:** The pores of the skin are generally large and visible. The skin is coarse to the touch and thick in texture. Oily skin tends to be prone to Acne.
2. **Dry Skin**: The pores are fine and not outwardly visible. The skin has a papery thin texture and feels fine to the touch.
3. **Normal Skin:** Neither dry nor oily to the touch, the pores are visible but not large.
4. **Combination Skin**: The skin is oily in areas called T-zones (forehead and nose) and dry in and around the cheeks.

What are visible the signs of damaged and aging skin?

1. Fine wrinkles around the mouth and eyes ("crow's feet")
2. Lentigos or (Benign brown spots associated with ultra-violet radiation from the sun) scattered on the forehead, nose and cheeks.
3. Focal hyper-pigmentation or discoloration on the upper lip, cheeks and forehead or (melasma) benign discoloration accentuated by the sun
4. Mottled pigmentation (Patchy skin color)
5. Loss of elasticity and collagen depletion resulting in deep wrinkles and sagging skin
6. Brown keratotic papules (Seborrheic Keratosis)
7. Red Scaly or keratotic papules or pre-cancerous (Actinic Keratosis)
8. Skin cancer (most commonly basal cell cancer and squamous cell cancer)

NOTE: The signs of aging and damaged skin are in part due to a genetic predisposition and are also the result of extrinsic factors such as over exposure to the sun, smoking, pollution and other life style stressors. People with lighter complexions are more susceptible to the harmful effects of external stressors, especially to ultra-violet rays produced by the sun.

Activar® Intensive Repair System with AC-11®

Question: Are the family of **Activar®** Products derived from natural ingredients?

Answer: The active ingredients in the Day, Night and Eye formulas are all natural. A small percentage of each product consists of preservatives and stabilizers that are derivatives of natural ingredients. These constituents are essential to providing an active and stable product. They can be found in luxury creams on the market today.

Question: Can I use the **Activar®** Creams with make-up?

Answer: The Day and Eye Creams absorb quickly and evenly in the skin and can be easily applied before make-up.

Question: What are the properties and benefits of each **Activar®** product?

Answer: Although the **Activar®** with AC-11® products shares many of the same advanced active ingredients they were formulated to provide the greatest effect when used as directed.

The Eye Cream was formulated to treat the sensitive skin under and around the eye and help diminish the appearance of dark circles and wrinkles. Rich in proven anti-aging ingredients including; Pepha-tight; an algae based anti-wrinkle and skin lightener, and MDI Complex; an active cosmetic ingredient that inhibits the breakdown of collagen and helps decrease the appearance of dark circles with Matrixmetalloproteinase (MMP) enzymes; giving the skin a younger, radiant and firmer appearance. De-liner™ is brand new technology used to smooth out fine lines and "crow's feet."

The Day Cream protects and maintains the cellular health of the skin which can be undermined by day time stressors including (sun exposure, fatigue, smoke and pollution). The Day Cream helps enhance the youthful and velvety appearance and radiance essential to healthy looking skin with Argireline® and White Tea Extract. The addition of Matrixyl®-3000 leads to new collagen production. Lipocol C and Liponate GC help maintain good skin metabolism and cellular health. The reparative and reformative function of the skin fundamental to cellular metabolism during day time assaults are enhanced by the presence of AC-11® and augmented by Vitamin A Palmitate a normalizer of cell function.

The Night Cream optimizes the natural repair mechanisms of the skin during the hours of rest. It should be noted, repair enzymes, hormones and bio-rhythms are among some of the factors that enhance repair during sleep. The Night Cream includes ingredients that help reduce cellular damage accumulated during the day. To augment the calmative properties that help induce repair the formula has a natural base of lecithin, the most common phosolipids found in all layers of the skin. AC-11® helps the skin's natural ability to repair DNA especially during sleep when the skin is generating its highest rate of repair. The Night Cream incorporates an intensive moisturizing base of Squalene and Hyaluronic Acid to rehydrate the skin. The formula also contains several additional proven actives including Cuivridone®, Argireline® and Matryxl®-3000 that smooth wrinkles and decreases pore size.

Question: Is it best to use the **Activar® Skin Renewal System** verses an individual product?

Answer: For best results, we recommend the system of Day, Night and Eye Repair Creams with one application of the Day and Nights Creams and two applications of the Eye Repair daily, in the morning and before bed.

Question: Do you recommend the use of ***Activar®* Skin Renewal System** if I suffer from Acne?

Answer: There are several natural oils and moisturizing agents in **Activar®** that may aggravate your acne condition.

Question: Should I use the **Activar® Skin Renewal System** if I am being treated by a physician for a skin condition?

Answer: It is strongly recommended that you consult your physician if you are being treated for a skin disorder before using **Activar®.**

Question: How can I be sure **Activar® Skin Renewal System** will reduce the visible signs of my wrinkles, reduce enlarged pores, help to fade age spots and discolorations and reverse sun damage?

Answer: To validate our results, a variety of men and women representing a cross section of skin types and races were selected to participate in a 30 day study using the **Visia Complexion Analysis System®**. The Visia System is specifically designed to measure:

1. UV Damage or damage to the skin due to exposure to the sun
2. Pore size
3. Wrinkles
4. Skin tone
5. Spots

Participants were measured for the 5 benchmarks listed before using **Activar® Skin Renewal System**. 30 days after using all three products as directed the results included:

A decrease in Pore size of 13 percent
Reduction in UV damage of up to 39 percent
Skin tone improvement of 31 percent
Decrease in fine lines and wrinkles of up to 60 percent
Decrease in spots of 15 percent

It should be noted that the benefits experienced varied among members in the study due to a variety of genetic and environmental factors.

Question: How does **Ceregenex** ensure that its products are safe for consumers?

Answer: Consumer safety is a top priority at **Ceregenex.** Studies have been conducted by the **Consumer Product Testing Company** of Fairfield, New Jersey under ICH Guideline E6 for Good Clinical Practice. All studies were conducted on male and female subjects varying in age and race, no visible signs of allergic reactions or irritations were observed.