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A New Paradigm for Reversal of Skin Aging

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BACKGROUND

It has been documented that chronic exposure to sunlight is the etiology of about 80% of the signs and symptoms of extrinsic skin aging. The most destructive sign of extrinsic aging is cutaneous malignancy. The mechanism of action is via oxidation reactions causing keratinocyte injury. Yet despite the introduction of high sun protection factor sunscreens and known antioxidant vitamin A and vitamin C containing skin care products, the incidence of cutaneous malignancy continues to climb. This epidemiology suggests other factors may contribute to these incomplete therapeutic successes.

Kligman and Lavker in 1988 elegantly demonstrated an inflammatory cellular response also involving mast cells surrounding papillary dermal fibroblasts. Mast cells are not documented to be activated by oxidation reactions, thus implying other inflammatory pathways are also involved in the signs of extrinsic skin aging.[1]

OBJECTIVES

Clinical trials were performed to document that optimizing stratum corneum permeability barrier function and reversing release and activation of chronic inflammatory factors improve the signs and symptoms of extrinsic aging. This goal was reached using two different formulations (ER and EIC), each having the same dual mechanisms of action. Neither test cosmeceutical contained vitamins A or C, soy, tea, kinetin, polyhydroxy or alpha hydroxy acids. These trials support a previous clinical trial presented at the American Academy of Dermatology Annual Meeting – 2006.[2]

METHODOLOGY

The three clinical trials involving 53 subjects were conducted between two different geographic sites with very different climates. The independent contract research group used trained clinical evaluators in these double blind, prospective, controlled trials of split face design conducted in the fall and winter. ER was compared to two commercial moisturizers and baseline in a 16 week and a 12 week trial. In both trials, subjects applied ER and the commercial moisturizer on opposite sides of the face twice daily. Clinical evaluations were performed at time 0, 2, 4, 8, 12 and 16 weeks in one trial and the first 5 time points in the second (n = 41). EIC was compared with idebonone 1% for 12 weeks, each applied twice daily. Clinical and bioinstrumentation derived readings were performed at 0, 6, and 12 weeks (n = 12). Safety, defined as adverse symptoms and signs of dermatitis, were assessed with both the two test cosmeceuticals and the control products.

RESULTS

ER was statistically significantly superior ($p<0.05$) to both baseline and control moisturizers of tactile roughness, fine lines, wrinkles, mottled hyperpigmentation, laxity and clarity at the 8, 12 and 16 week time points. At two weeks, statistical significant superiority was achieved with ER of tactile roughness and fine lines. The numerical results are superior to other products containing active cosmeceutical ingredients. The clinical results are published as in Chart I, including glycolic acid (GA), polyhydroxy acid (PHA) and kinetin. No subjects experienced any adverse reaction.

CHART I (% Change By Week 12)

Parameter	ER	GA	PHA	KINETIN
Fine Lines	38	20	22	10
Wrinkles	33	13	10	--
Roughness	64	43	42	48
Hyperpigmentation	34	--	--	--
Laxity	21	--	--	--
Clarity	+91	+30	+32	--

EIC achieved clinical statistically superior ($p<0.05$) over baseline and idebenone 1% (I) at the 6 week time point showed decrease in shallow wrinkles, roughness, hyperpigmentation, laxity and improvement in clarity. Furthermore, EIC produced statistically significant superior dermal extensibility at 12 weeks. The clinical results are published as in Chart II.

With regard to safety, idebenone induced contact irritant dermatitis in 30% of the subjects by 6 weeks with one subject dropping out due to autoeczematization including spreading to the EIC treated side of the face. No other subjects developed symptoms or signs of adverse reactions at the EIC site.

CHART II (% Change By Week 6)

Parameter	EIC	I
Shallow Wrinkles	26.1	9.4
Roughness	40.6	28.0
Hyperpigmentation	12.2	6.2
Laxity	10.0	5.3
Clarity	+34.9	+28.1
Dermal Extensibility*	19.4	10.2

* % Change by week 12

CONCLUSIONS

These double blind, prospective, controlled trials using two different finished, marketed cosmeceutical products with the same mechanism of action, but different active ingredients appear to prove a new paradigm for reversal of the signs and symptoms of skin aging. This paradigm utilizes two mechanisms of action: optimization of the stratum corneum permeability barrier and reversing/preventing chronic inflammatory factors. The fact that two products with different active ingredients produce similar clinical results proves this paradigm is a clinical reality. In addition, these studies strongly suggest products utilizing this new paradigm are clinically more effective than accepted cosmeceutical active ingredients for reversing signs of extrinsic aging. Moreover, the new paradigm is more effective and safer than most potent antioxidant products on the market, confirming that suppression of multiple inflammatory pathways is more effective than blocking the single oxidation path. Finally, products with this new paradigm appear safer than a single antioxidant product.

The test products ER and EIC do not contain retinol, alpha hydroxy or polyhydroxy acid, soy, tea or ascorbic acid. ER consists of a blend of date, flax, meadowfoam and avocado highly purified extracts to ameliorate inflammatory factor release and activation in a physiologic lipid rich formula. EIC contains hydrolyzed yeast tripeptide and potato tetrapeptide blended with ursolic acid and azelates, also in a similar formulation.

In conclusion, this new paradigm for reversing skin aging should be considered by all physicians and skin care professionals when recommending therapy for extrinsic skin aging.

REFERENCES

1. Lavker R, Kligman A. Chronic heliodermatitis: A morphologic evaluation of chronic actinic dermal damage with emphasis on the role of mast cells. J Invest Dermatol. 1988; 90: 325-330.
2. Sigler M, Thornfeldt C. A cosmeceutical with novel mechanisms of action effectively reduces signs of extrinsic aging; Poster Exhibit P1128. 2006 American Academy of Dermatology Annual Meeting - San Francisco, CA.

DISCLOSURE
This study was sponsored by Episciences, Inc. of Boise, ID, founded by Carl Thornfeldt, M.D., President and CEO. It was conducted by the independent contract research organization, Stephens & Associates, of Colorado Springs, CO and Dallas, TX.