CLINICAL EVALUATION OF A PRESCRIPTION SKIN THERAPY SYSTEM DESIGNED TO TREAT FACIAL PHOTODAMAGE: EFFICACY AND SAFETY COMPARISONS TO 0.1% TRETINOIN REGIMEN, 4% HYDROQUINONE REGIMEN, AND OVER-THE-COUNTER (OTC) REGIMEN

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ABSTRACT

INTRODUCTION: This 24-week study in 301 subjects examined the clinical efficacy and safety of a proprietary system (Prescription Skin Therapy System) composed of a specific protocol of cleanser, toner, α-hydroxy acid, tretinoin, hydroquinone and SPF (Group 1), compared with a 0.1% tretinoin regimen, including cleanser and SPF 30 (Group 2), 4.0% hydroquinone regimen, including cleanser and SPF 30 (Group 3) and the most common over-the-counter (OTC) products recommended by physicians—cleanser, moisturizer and SPF 30 (Group 4).

METHODS: Facial photodamage (perioral wrinkles, periocular wrinkles, facial wrinkles, hyperpigmentation, clarity, sallowness, tactile roughness, and laxity) and irritation (erythema, edema, scaling, papular rash, burning, stinging, itching, and tightness) were assessed by investigative clinical graders at baseline and 1, 6, 12, 18, and 24 weeks of treatment. Digital photography, ultrasound scans, silicone replicas, and full-thickness facial biopsies were also performed.

RESULTS: The Prescription Skin Therapy System was significantly more effective ($P \leq 0.05$) than the other three treatments in all seven variables as demonstrated by change from baseline in evaluations at 12 weeks and 24 weeks (Figures 1 and 2).

CONCLUSIONS: The Prescription Skin Therapy System outperformed the other three regimens (Drug or OTC) at both 12 weeks and 24 weeks.

INTRODUCTION

- 75% of physicians recommend over-the-counter (OTC) skin care products to their patients. (The US Professional Skin Care Market 2003, Kline & Company)
- Since 1997, the number of interventions for facial photodamage in the US has increased 293%—an 87% increase in surgical procedures and a 471% increase in nonsurgical procedures.[1]
- Although studies have established the efficacy and safety of monotherapies and combination therapies, few have compared the clinical benefits of commonly prescribed drug and OTC regimens with those of "systems" in patients with photodamage.[1]

METHODS AND PROCEDURES

Study Design

- A total of 301 women with Fitzpatrick skin types I to IV were randomized into four treatment groups in a 1:1:1:1 ratio (Table 1).
  - Group 1: Prescription Skin Therapy System including a cleanser, toner, tretinoin, hydroquinone, α-hydroxy acids, and sunscreen (n=71)
  - Group 2: 0.1% tretinoin with cleanser and moisturizer with sunscreen (n=74)
  - Group 3: 4.0% hydroquinone with cleanser and moisturizer with sunscreen (n=79)
  - Group 4: Over-the-counter (OTC) regimen including cleanser and moisturizer with sunscreen (n=77)
- Randomization was adjusted to ensure the groups were balanced for the following:
  - Age 38–48, 49–56, or 57–65 yr
  - Fitzpatrick skin type I, types II and III, or type IV
  - Presence of perioral fine wrinkles (≥50% of participants had "smoker's lines")
  - Skin type normal, normal to dry, normal to oily, dry, or oily
- A subgroup of patients (n=40) agreed to have two facial skin biopsy samples taken; ten were placed randomly into each of the four treatment groups.
- The study was conducted at two sites in Texas (Carrollton and Arlington).

Efficacy Evaluations

- **Performance Variables** (Visits 2, 3, 6, 7, 8, and 9)—The investigator examined each participant's face for perioral fine wrinkles, periocular fine wrinkles, facial fine wrinkles, mottled hyperpigmentation, clarity, sallowness, tactile roughness, and laxity (Table 2). Digital photography was used at Visits 2, 7, and 9 to document changes in performance variables. Two images of each face (visible and cross-polarized light) were taken using a Fuji FinePIX ProS2 camera with AF Micro Nikkor lens (zoom 70–180 mm).
- **Ultrasound Measurements** (Visits 2, 7, and 9)—Skin density measurements were taken on the temple area of the selected side of the face using a DUB20 (Taberna, Pro Medicum, AG) ultrasound unit.
- **Silicone Replicas** (Visits 2, 7, and 9)—Silicone replicas were taken on the crow's foot area and upper lip of the selected side of the face to document fine perioral and periocular wrinkling.
- **Skin Biopsy** (Visits 2 and 9)—Ten participants from each treatment group had 2 mm full-thickness punch biopsy samples obtained on the right or left cheek; specimen histology was analyzed by dermatopathologists, who specifically assessed stratum corneum compaction, granular cell layer thickness, epidermal thickness, spongiosis, epidermal pigmentation, dermal pigmentation, collagen, elastin, and GAGs/extracellular matrix.

Safety and Tolerability Evaluations

- **Irritation Parameters** (Visits 2, 3, 6, 7, 8, and 9)
  - Investigators assessed objective signs of cutaneous irritation (erythema, edema, scaling, and papular rash) and the severity of erythema (burning, stinging, itching, tightness, and tingling) on the following scale: 0=none, 1=mild, 2=very mild, 3=moderate, and 4=severe.
  - Participants assessed subjective sensation (burning, stinging, itching, tightness, and tingling) on the following scale: 0=none, 1=mild, 2=moderate, and 3=severe (half points were used as needed).

Table 1. Study Treatments

Treatment Group	Morning	Evening
Group 1 (n=71) ***Prescription Skin Therapy System (Obagi Nu-Derm System)***	Cleanser/Toner 4.0% hydroquinone α-hydroxy acids SPF 15 + 4.0% hydroquinone	Cleanser/Toner 4.0% hydroquinone 0.1% tretinoin/4.0% hydroquinone
Group 2 (n=79) ***0.1% tretinoin regimen***	Cetaphil Daily Facial Cleanser Neutrogena Healthy Defense Moisturizer SPF 30	Cetaphil Daily Facial Cleanser 0.1% tretinoin cream Neutrogena Healthy Defense Moisturizer SPF 30 (as needed)
Group 3 (n=74) ***4.0% hydroquinone regimen***	Cetaphil Daily Facial Cleanser Neutrogena Healthy Defense Moisturizer SPF 30	Cetaphil Daily Facial Cleanser 4.0% hydroquinone cream (no SPF) Neutrogena Healthy Defense Moisturizer SPF 30 (as needed)
Group 4 (n=77) ***over-the-counter (OTC) regimen***	Cetaphil Daily Facial Cleanser Neutrogena Healthy Defense Moisturizer SPF 30	Cetaphil Daily Facial Cleanser Neutrogena Healthy Defense Moisturizer SPF 30 (as needed)

Table 2. Skin Assessment Criteria

Performance Variables	Grading Scale
Perioral fine wrinkles	0=none 10=extensive wrinkling
Mottled hyperpigmentation	0=no hyperpigmentation 10=extensive hyperpigmentation
Laxity	0=firm/unpliable skin 10=loose/pliable when manipulated
Periocular wrinkles	0=none 10=extensive wrinkling
Sallowness	0=none 10=extensive sallowness

RESULTS

Demographics

- A total of 301 participants completed the study; all were women (mean age 52 yr) and the majority were caucasian (Table 3).

Efficacy

- **Performance Variables**—The Prescription Skin Therapy System was significantly more effective ($P \leq 0.05$) than the other three treatments in all seven variables as demonstrated by the change from baselines in evaluations at 12 weeks and 24 weeks (Figures 1 and 2). Further, results with the Prescription Skin Therapy System at 12 weeks were significantly superior to results with the tretinoin and hydroquinone regimens at 24 weeks.
- **Ultrasound Measurements**—The Prescription Skin Therapy System showed significantly greater improvement ($P \leq 0.05$) in the mean density scores than the tretinoin regimen, hydroquinone regimen, and the over-the-counter (OTC) regimen at 24 weeks (Table 4).
- **Silicone Replicas**—The Prescription Skin Therapy System and the tretinoin regimen produced the best improvements in smoothing of periorbital and periocular fine lines and wrinkles ($P \leq 0.01$).
- **Skin Biopsy**—Greater improvement was seen in cornified layer compaction with the Prescription Skin Therapy System and tretinoin regimen than with the hydroquinone and the nonprescription regimens.

Safety and Tolerability

- Participants treated with the Prescription Skin Therapy System showed the greatest increases ($P \leq 0.05$) in erythema and scaling at weeks 1, 6, 12, and 18; however, by week 24, participants treated with the Prescription Skin Therapy System and the tretinoin regimen had equivalent ratings on irritation parameters, with similar findings for side effects such as edema, papular rash, stinging, itching, and tightness.

Table 3. Demographics of Study Population

		All Participants (n=301)	Group 1 (n=71)	Group 2 (n=74)	Group 3 (n=79)	Group 4 (n=77)
Age, yr	Mean Age	52.06	51.36	52.31	52.94	52.57
	Minimum Age	38.17	39.33	38.72	38.72	38.17
	Maximum Age	65.90	64.63	65.85	65.90	65.84
Ethnicity, n (%)	Caucasian	274 (91.02)	65 (91.54)	69 (93.24)	74 (93.67)	66 (85.71)
	Other	27 (8.96)	6 (8.45)	5 (6.76)	5 (6.33)	11 (13.31)

Table 4. Improvements in Ultrasound Density Scores

Treatment Group	Baseline (Visit 2)	Week 24 (Visit 9)	*P* Value	Δ Value
Group 1 (n=71)	42.80	53.10	⇑	10.30
Group 2 (n=74)	44.86	50.05	⇑	5.19
Group 3 (n=79)	43.08	48.53	⇑	5.45
Group 4 (n=77)	42.61	44.42	⇑	1.81

⇑ Indicates a statistically significant ($P \leq 0.0001$) increase *(improvement)* compared with baseline values.

Figure 1. Comparative Efficacy at 12 Weeks

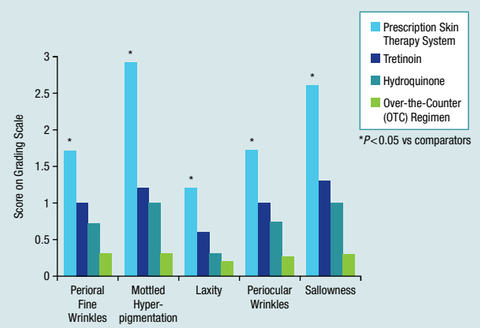
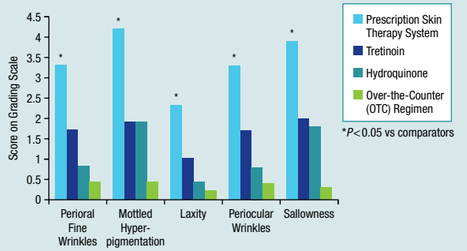


Figure 2. Comparative Efficacy at 24 Weeks



CONCLUSIONS

- The Prescription Skin Therapy System significantly improved perioral fine wrinkles, periocular fine wrinkles, facial fine wrinkles, mottled hyperpigmentation, clarity, sallowness, tactile roughness, and laxity compared with the commonly prescribed regimens of tretinoin and hydroquinone and the over-the-counter (OTC) regimens.
- The proprietary Prescription Skin Therapy System composed of a protocol of cleanser, toner, α-hydroxy acids with 0.1% tretinoin, 4.0% hydroquinone, and SPF has statistically superior efficacy in the treatment of photodamage than other tested therapies.
- The Prescription Skin Therapy System was well tolerated when used under appropriate supervision.
- Other efficacy parameters will be described in a future publication.
- To optimize outcomes in individuals with fine lines and wrinkles plus laxity characteristic of photodamaged skin, clinicians should consider treatment with drug regimens or more ideally, with the Prescription Skin Therapy System.

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