

A Silymarin Antioxidant Serum Improves Facial Acne Alone and as Part of a Treatment Regimen

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ABSTRACT

Background: Silymarin is an antioxidant that can protect against free radicals that cause premature signs of aging and oil oxidation that may contribute to breakouts.

Aims: The objective of these studies was to evaluate a silymarin antioxidant serum alone and in combination with a prescription acne treatment regimen in improving facial appearance in blemish-prone skin.

Methods: Two international studies were conducted. A 12-week study in Brazil enrolled 56 subjects to examine the effect of silymarin antioxidant serum on facial acne. Clinical grading on acne lesions, skin tone, clarity, and postinflammatory hyperpigmentation (PIH) were conducted. In addition, consumer self-assessment, analysis for markers of lipid peroxidation, and sebumeter analysis were completed. Another United States (US)/German study enrolled 40 subjects who were on topical prescription acne medications to which silymarin antioxidant serum was added. Acne lesion counts, tolerability, and facial appearance assessments were conducted in this study.

Results: The Brazilian study demonstrated a 45% reduction in inflammatory lesions and a 43% reduction in noninflammatory lesions after 12 weeks of silymarin antioxidant serum use. In addition, sebumeter testing showed a 16% reduction in oiliness at week 1. The US/German study showed the benefits of the serum in persons already on prescription acne therapy by reducing facial erythema by 60%, dryness by 49%, and scaling by 67%.

Conclusion: Silymarin is shown in clinical testing to have significant benefits in reducing lipid peroxidation, oiliness, and PIH, and in improving key markers of skin aging. Additionally, the serum can be used alone or as an adjunctive treatment in acne therapy to further benefit aging, acne-prone skin.

J Drugs Dermatol. 2024;23(4):233-238. doi:10.36849/JDD.8120

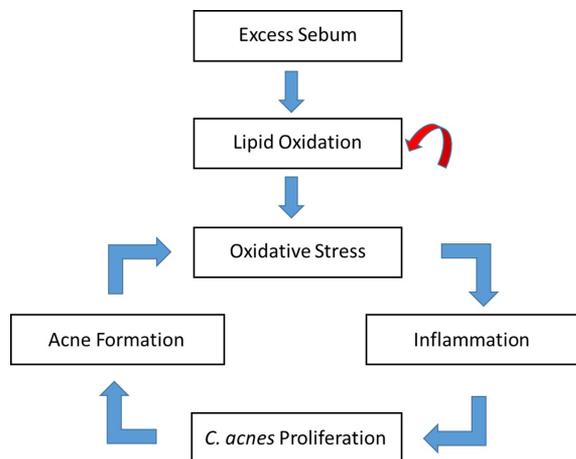
INTRODUCTION

Acne is an inflammatory condition common in adolescents, but blemish-prone skin can persist into adulthood.^{1,2} The pathogenesis of acne is characterized by increased sebum production, follicular hyperkeratinization, *C. acnes* colonization, and inflammation, which manifest as inflammatory and noninflammatory acne lesions. Acne is believed to have an underlying genetic component, but it can be influenced by a wide variety of factors including age, gender, ethnicity, hormones, diet, pollution, climate, and stress.³⁻⁷

A link has been proposed between sebum and acne, with sebum oxidation perhaps contributing to enhanced formation of lesions.^{8,9} Acneic skin is reported to have both higher levels of oxidative stress and lower levels of antioxidants than healthy skin.¹⁰ Additional oxidative environmental factors, such as ultraviolet (UV) radiation and pollution, generate free radicals

that exacerbate the condition. Oxidative stress, particularly lipid peroxidation, contributes to inflammation, which creates a favorable environment for acne-causing bacteria (Figure 1). It has been proposed that topical antioxidant application can improve this environment and help reduce the prevalence of acne.¹¹⁻¹⁶

Silymarin is a standardized extract from the seeds of the milk thistle plant (*Silybum marianum*) which typically contains 70% to 80% of an isomeric mixture of flavonoid complexes called flavonolignans. The main flavonolignans comprising silymarin are silybin, isosilybin, silychristin, dehydrosilybin, and silydianin, in addition to the flavonoid taxifolin. The highest concentration, comprising roughly 50% to 60% of silymarin, is silybin, which is the major bioactive component of the extract. Silymarin is a powerful antioxidant owing to the complimentary free radical scavenging abilities of the various

FIGURE 1. The role of lipid oxidation in the acne cycle and opportunity for antioxidant intervention.

flavonolignan isomers. As such, it is reported to have a range of biological activities, including the ability to help reduce lipid peroxidation.¹⁷⁻¹⁹

A formula of 0.5% silymarin is combined with 15% L-ascorbic acid and 0.5% ferulic acid to form a triple-antioxidant serum that may provide protection against free radicals that cause both premature signs of aging and oil oxidation that may contribute to acne.²⁰ The oil-free serum also contains 0.5% salicylic acid, a well-known monographed acne active. A comprehensive efficacy clinical and international tolerance assessment were designed to evaluate the effectiveness of the silymarin antioxidant serum across parameters of aging, as well as acne reduction when used alone and as part of an acne treatment regimen.

MATERIALS AND METHODS

The initial efficacy study was a 12-week, single center, blinded clinical study conducted in Brazil (CIDP Brasil, Rio de Janeiro, Brazil) on 56 male and female subjects aged 18 to 48, with Fitzpatrick skin types ranging from II to V. The enrolled subjects presented with mild-to-moderate acne, lack of clarity, uneven skin tone, and postinflammatory hyperpigmentation or erythema (PIH/PIE). Subjects applied the serum to the face once daily for the duration of the study in conjunction with a mild cleansing bar and sunscreen. Clinical grading, tolerance evaluations, sebumeter measurements, and subject self-assessments were conducted at baseline and weeks 1, 4, 8, and 12. A randomized subset of the panel (N=30) had sebum sampled from the forehead by swabbing at baseline, week 4, and week 12, which was analyzed for lipid content.

In addition, consumer perception was evaluated upon immediate application and after 1, 2, 4, 8, and 12 weeks of use. Perception was measured on a scale of 1 through 9, where 1 was the most

TABLE 1.

Prescribed Acne Medications

Topical Benzoyl Peroxide

Adapalene

Tretinoin

Tazarotene

Clindamycin

Oral Minocycline

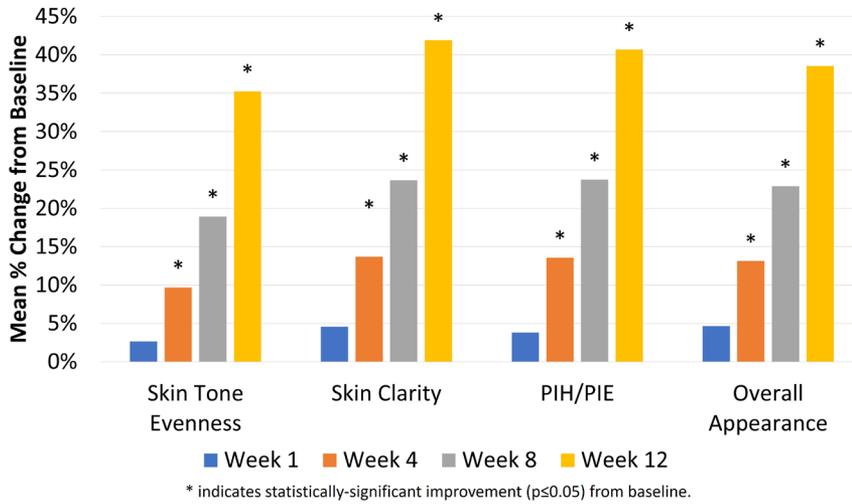
negative response and 9 was the most positive response. The results are expressed as a percentage of favorable responses (score ≥ 6).

A second international study explored the tolerability of the silymarin antioxidant treatment when used in combination with a variety of prescription acne medications. Forty healthy females aged 18 to 50 of all Fitzpatrick skin types, who were currently using prescription topical acne medications, were enrolled in this international study.²¹ Prescribed acne medications are listed in Table 1. To their acne treatment regimen, subjects added a silymarin-containing antioxidant facial serum. The investigators from the United States (Zoe Diana Draelos MD, Dermatology Consulting Services, PLLC, High Point, NC) and Germany (Martina Kerscher MD) rated the subjects for facial dryness, erythema, and edema; while the subjects rated themselves for the facial sensory attributes of stinging, tingling, itching, and burning. All assessments were conducted on a 4-point ordinal scale along with facial photography at baseline and week 4. Subjects also completed a self-assessment questionnaire regarding skin clarity improvement, skin radiance improvement, skin oil presence, and product perception after 1 and 4 weeks of product use.

RESULTS

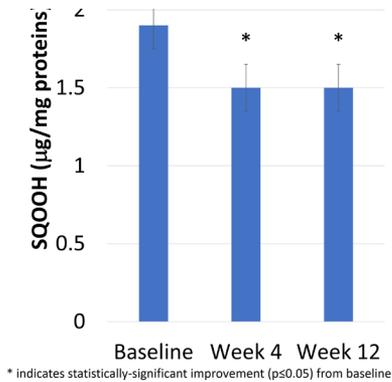
For the efficacy study, 12-week results showed statistically ($P<0.001$) significant improvement in skin clarity by 42%, PIH by 41%, skin tone evenness by 35%, and overall appearance by 39% after applying the silymarin serum (Figure 2). In addition, sebumeter testing showed a 16% reduction in skin surface oil at week 1 ($P<0.001$). Furthermore, analysis of the collected sebum samples showed a significant reduction in squalene peroxide at both week 4 and week 12 (Figure 3). Global lesion count showed a modest decreasing trend at week 4, but significant improvement by week 8 and week 12 driven by a reduction in both inflammatory and non-inflammatory lesions. The investigator's global assessment (IGA) of acne severity also showed a significant improvement of 27% at week 12. There was a 45% reduction in inflammatory and a 43% reduction in noninflammatory lesions (Figure 4). Figure 5 illustrates the improvement observed in skin appearance and PIH with the silymarin antioxidant serum. Consumer perception received

FIGURE 2. Bar graph showing the improvement of evaluated skin attributes.



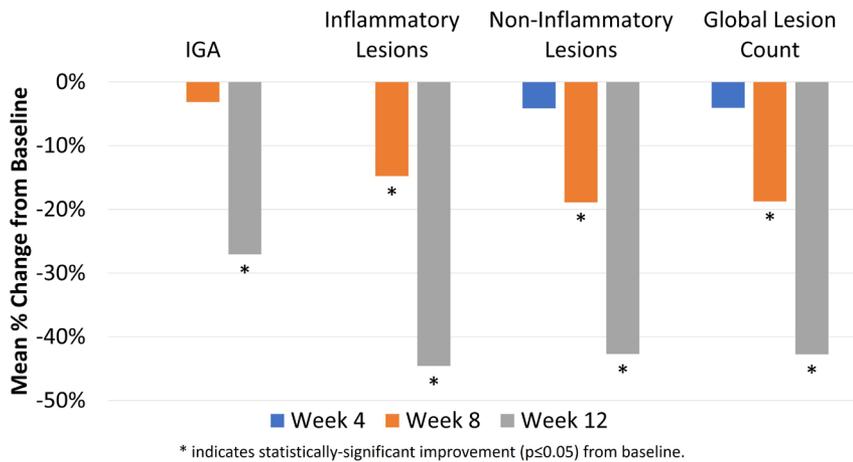
The changes are statistically significant ($P < 0.05$).

FIGURE 3. Bar graphs showing sebum peroxidation over time.



Asterisks indicate statistical significance ($P < 0.05$).

FIGURE 4. Bar graph showing improvement of evaluated acne parameters. The changes are statistically significant ($P < 0.05$).



The changes are statistically significant ($P < 0.05$).

an overall favorable response (>50% of subjects rating ≥ 6). Additionally, the silymarin antioxidant serum was well-tolerated by the subjects.

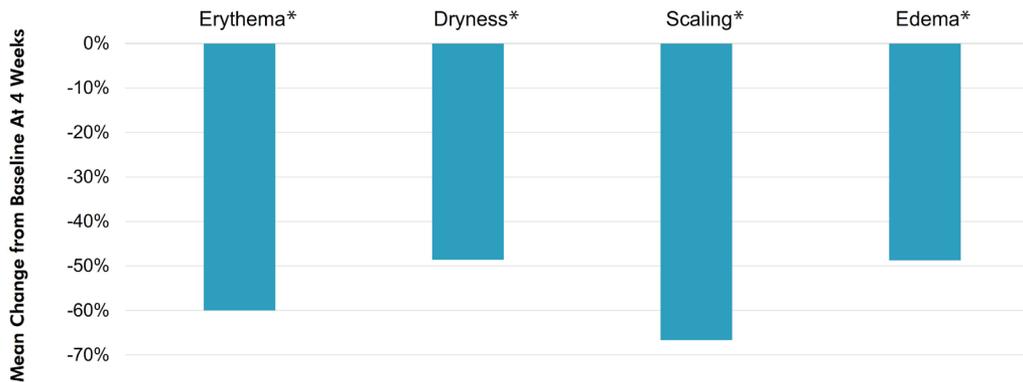
In the second international study, after 4 weeks of adding the silymarin antioxidant serum to the subjects' prescribed regimen, the investigator's assessment showed a statistically significant reduction in facial erythema, dryness, and scaling

(Figure 6). Additionally, subjects noted a statistically significant reduction in facial tightness and dryness (Figure 7). Photographic visualization also demonstrated facial skin tolerability including erythema, dryness, and scaling (Figure 8). After one week of use, 70% of subjects agreed the serum made their skin feel less oily, 58% felt the serum improved their skin clarity, and 50% felt serum improved skin radiance. Over half the subjects desired to continue using the serum after completion of their prescription acne therapy.

FIGURE 5. Photographic visualization of skin attributes including overall skin appearance, clarity, and postinflammatory hyperpigmentation at various timepoints.

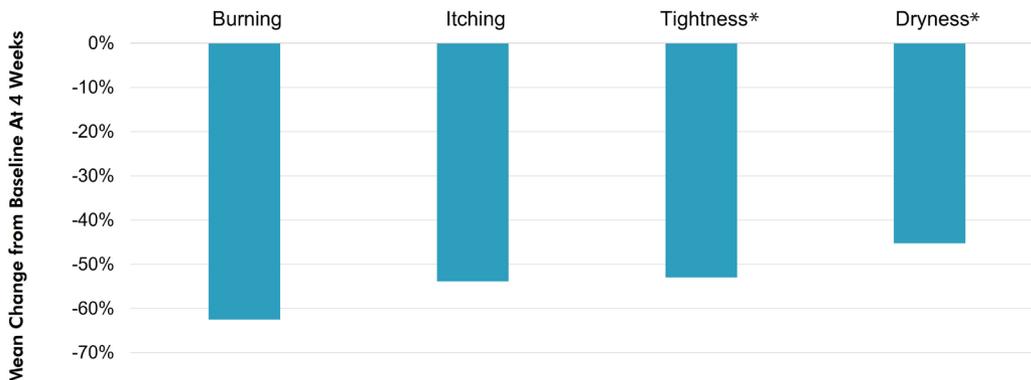


FIGURE 6. Bar graph showing investigator-assessed reductions in key facial symptoms.

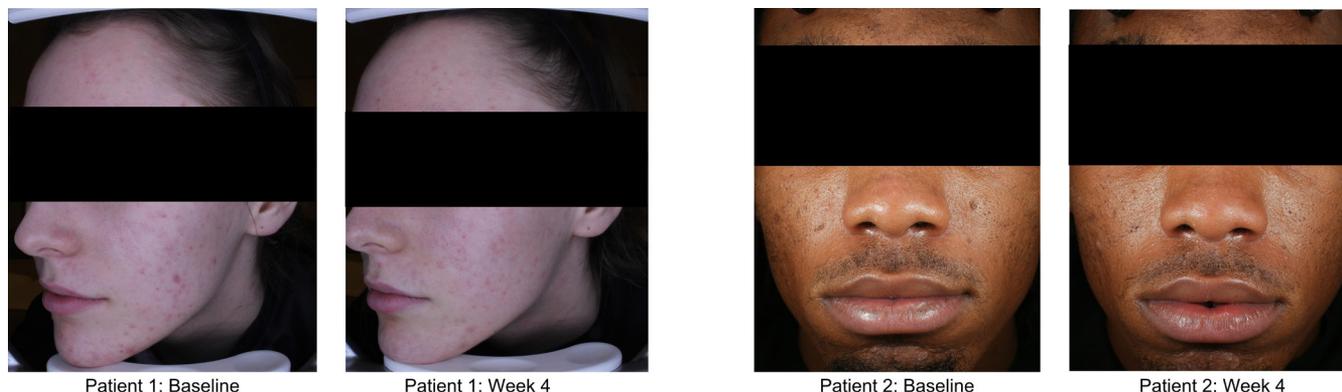


Asterisks indicate statistical significance ($P < 0.05$).

FIGURE 7. Bar graph showing subject-assessed reductions in facial sensory attributes.



Asterisks indicate statistical significance ($P < 0.05$).

FIGURE 8. Representative photos of facial skin tolerability, including erythema, dryness, and scaling.

DISCUSSION

Acne is a condition with complex etiology. It often persists into adulthood and the incidence in mature women is increasing. There is a need for new topical treatments that address underlying factors that have been associated with the disease. One of the key contributors to the oxidative stress theory of acne is a redox imbalance due to lipid peroxidation within the sebum and progressing through the various stages of comedogenesis. Since antioxidants are well known to help prevent lipid peroxidation, there is an opportunity for topical supplementation to mitigate the disease progression.

The results from the Brazilian study showed that a topical serum containing 0.5% silymarin, 15% vitamin C, 0.5% ferulic acid, and 0.5% salicylic acid was effective in reducing facial acne and improving associated skin attributes such as clarity, tone evenness, and pigmentation. While some skin benefits are seen rather quickly, the strongest improvement in lesional acne is observed with continued usage. This suggests that the fundamental stabilization of lipid peroxidation may be an important underlying strategy for daily management of oily, acne-prone skin while also improving overall skin appearance.

The study demonstrated the fundamental ability of the treatment to broadly decrease the IGA and inflammatory and noninflammatory lesion counts after 12 weeks of use. Silymarin is known to reduce the production of inflammatory mediators produced by *C. acnes* and also inhibit the migration of neutrophils to the inflammatory site, preventing the release of reactive oxygen species, reactive nitrogen species, and proteolytic enzymes.²² This may be a possible mechanism of action for its observed benefit in this acne research.

Additionally, in the US/German study, the product was found to be well-tolerated when used as part of a prescription regimen. After 4 weeks of use, more than half the subjects felt that the

silymarin antioxidant serum improved skin clarity and desired to continue using the serum after completion of their prescription acne therapy.

The topical silymarin antioxidant serum addresses an emerging acne therapy need with both acne and aging concerns. Thus, a silymarin antioxidant serum can fulfill anti-aging and acne needs on its own or with prescription acne treatment with favorable tolerability. This novel silymarin antioxidant serum was shown to have a significant benefit in reducing acne alone and as part of a cosmeceutical acne regimen or prescription acne treatment. In addition, clinical testing demonstrated significant improvement in skin attributes, providing a possible solution for aging concerns in oily, acne-prone skin.

DISCLOSURES

ZDD and MK received a research grant from L'Oreal to conduct the research presented in this manuscript. HC, SW, and SL are employees of L'Oreal.

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