ANTINFLAMMATORY, ANTIMICROBIAL, COMEDOLYTIC EFFECTS OF A TOPICAL PLANT COMPLEX TREATMENT IN ACNE VULGARIS: A CLINICAL TRIAL.

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Summary

Acne is a disease of the pilosebaceous unit and it may be characterized by non inflammatory lesions, such as comedones and cysts and/or by inflammatory lesions such as erythematous papules, pustules, nodules. The lesions may or may not resolve with scars. Three major factors are involved in the pathogenesis of acne: increased sebum production, an abnormality of the microbial flora, cornification of the infundibula duct. These three components represent the target of different plant extracts, which may play an important role in inducing comedolytic, antimicrobial effects and also in improving pitted scars.

This study was aimed at evaluating the efficacy of a topical plant complex treatment in acne vulgaris in 30 volunteers. These volunteers were divided in two groups: 15 received only the topical treatment and 15 received topical treatment plus oral placebo capsules. The instrumental investigation evaluated the following parameters during 90 days: skin hydration, transepidermal water loss, erythema, skin brightness, sebum on skin surface, scars.

The statistical analysis of data at the end of this clinical trial underlined that the topical plant complex product improves the clinical appearance of acne.

Riassunto

L’acne è una malattia dell’unità pilosebacea e può essere caratterizzata da lesioni non infiammatorie, come comedoni e cisti e/o da lesioni infiammatorie come papule eritematose, pustole, noduli. Le lesioni in alcuni casi possono risolversi con cicatrici. Sono tre i maggiori fattori implicati nella patogenesi dell’acne: ipersecrezione sebacea, alterazione della normale flora microbica, iperkeratosi infundibolare. Questi tre fattori rappresentano l’obiettivo di differenti estratti vegetali, che possono svolgere un importante ruolo nella comedolisi, possono avere effetti antimicrobici e migliorare le cicatrici più superficiali.

Lo scopo di questo studio è stato quello di valutare l’efficacia di un complesso vegetale topico nel trattamento dell’acne vulgaris in 30 volontari. Questi soggetti sono stati suddivisi in 2 gruppi: 15
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hanno ricevuto solo il trattamento topico e 15 il trattamento topico più le capsule placebo. L’indagine strumentale consisteva nel valutare l’andamento, durante 90 giorni, dei seguenti parametri: idratazione della pelle, TEWL (transepidermal water loss), eritema, luminosità, sebo sulla superficie della pelle, repliche (impronte) cutanee. L’analisi statistica dei risultati alla fine dello studio clinico ha indicato che questo prodotto migliora l’aspetto clinico dell’acne.
INTRODUCTION

Acne is characterized by polymorphic noninflamed (comedones) or inflamed lesions (papules, pustules, nodules), which occur predominantly on the face, but also on the back and chest. Although acne is present mainly during teenage years, it may continue as a clinical problem into twenties and older.

Typical lesions of mild to moderately severe acne vulgaris (comedones, small papules, seborrhoea) in adolescents come and go for several years, sometimes resolving with residua, i.e., pitted scars and patulous follicle on the nose and malar region.

There is no single cause of acne, and several factors seem to play important pathogenetic role. Active sebaceous glands are a prerequisite for the development of acne; in fact acne patients excrete abnormally high levels of sebum that may result from an high androgen production or increased availability of free androgen. Anyway there is an amplified target response, i.e. sebum production. Moreover acne patients show ductal hypercornification which clinically presents as comedones. The presence of abnormal environment (sebum excretion rate and ductal cornification) causes an alteration of the microbial flora (1-7).

On the basis of these main etiologic factors, treatments should be carried out through substances that are both effective in reducing the excessive release of the sebum and in regulating cornification of the infundibula and in improving the cutaneous microflora and facilitating healing of lesions.

The purpose of this study is to evaluate the efficacy of a topical treatment in acne vulgaris in a group of 30 selected volunteers with 90-day clinical trial.

In particular, a formulation containing the following active principles, Prepared by Medestea International laboratories, based in Torino, Italy, has been tested: lauric acid, standardized lipophilic extract of Krameria trianda Ruiz, 18-á glycyrrhctic acid in phytosome form, standardized lipophilic extract of Serenoa repens and Centella asiatica (pure triterpenic fraction).

The instrumental investigation measured basal (prior to treatment), intermediate (after 7-30-60 days) and final (after 90 days) values of the following biophysical cutaneous parameters: skin hydration, Transepidermal water loss, erythema and skin brightness, sebum and imprint of skin surface (8-17).

MATERIALS

Thirty subjects (8 male and 22 female, average age 24.62 years) presenting different degrees of facial acne (slight, moderate, severe) were included in this study.

The volunteers were divided into two groups in which one half received only the topical treatment and the other half received the topical treatment associated with an orally administered product (placebo). Volunteers were subjected to a clinical evaluation before (T0) and after treatment (T1) (Tab. I). During the trial, volunteers did not use other anti-acne products.

Degree of skin hydration was evaluated by a cornometer CM 820 PC (Courage & Kazhaka®, Koln, Germany). The instrument measures the dielectric constant of the stratum corneum and is constituted by a cylindrical sensor (measuring probe) connected by a spiral coil. Measurements are taken by placing the measuring head on the skin: after about 8 seconds, the water content is measured with the simultaneous display of the hydration value.

An evaporimeter (evaporimeter EP 1 Servomed®, Sweeden) is used to assess Transepidermal water loss (TEWL). This instrument measures the flow of water vapor through a given surface (unit), by means of the variations of water concentration in the atmosphere near the stratum corneum. Measurements are taken 30' after positioning the probe on skin surface.
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Table I
Clinical criteria for evaluating five degrees of acne severity in the two groups of volunteers.

<table>
<thead>
<tr>
<th>Topical treatment</th>
<th>T0</th>
<th>T1</th>
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<tbody>
<tr>
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<td>n° subjects</td>
<td>n° subjects</td>
</tr>
<tr>
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<td>0</td>
</tr>
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<td>8</td>
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<td>severe</td>
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<table>
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<th>T1</th>
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<td>n° subjects</td>
<td>n° subjects</td>
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<td>0</td>
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<tr>
<td>severe</td>
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</table>

Index of erythema and skin brightness was evaluated through the use of a colorimeter (Minolta Chroma Meter Cr-200°), which uses a geometry with diffuse illumination with an observation angle at 0° to obtain a reading correlated to the surface examined. The illumination chamber of the instrument is a cylinder with a conical opening of 8 mm in diameter directed towards the skin surface. The vertically reflected light on the measurement surface is captured by an optic fiber cable for the analysis of the color.

The sebumetric evaluation is performed by a sebumeter Sm810 Pc° (Courage and Khazaka, Koln-West Germany). An opaque synthetic band is applied on the area of skin to be tested for 30 sec. The surface of the band of about 64 mm2 becomes more transparent as the sebum deposits. This variation of transparency to the light represents the value of the skin sebum and is measured by means of a photometer. The values obtained are expressed in sebometric units which are convertible in micrograms per surface unit.

The imprint of skin surface, obtained by skin replica using silicone (Silflo°), was studied by an image analyzer Philips NMS 8280. Then, the images were elaborated by a computer which gives values about microrelief and deep furrows.

At the end of the trial, the data were analyzed by paired and unpaired t-student test.

RESULTS

The values of hydration (Fig. 1) of the stratum corneum in subjects only using topical products were significantly increased by 16.94%, after 3 months of treatment (t-test = 0.013), ranging from a basal value of 67.52 to a final value of 78.96.

![Fig. 1: Graphic presentation of the cutaneous hydration in the two groups of volunteers.](image-url)
An increase of the hydration parameter, equal to 23.63%, was found also in the volunteers who had associated the oral product to the topical product. In this case, there was an increase from a basal value of 59.32 to a final average value of 73.34, with significant variations already after 1 month of treatment (t-test bas/1 month = 0.004; t-test bas/2 months = 0.003; t-test Bas/3 months = 0.0001).

The Transepidermal Water Loss (TEWL) (Fig.2) was significantly decreased by 37.81% (t-test = 0.039) in the first group after 3 months of treatment (average basal value = 15.89, average final value = 9.88). A significant reduction was recorded also after two months of treatment (t-test = 0.048; average value after 2 months = 10.27).

A significant decrease (t-test = 0.002) equal to 19.54% was also recorded in the second group after three months of treatment (basal average value = 10.54; final average value = 8.48).

Nevertheless, it is important to note a significant reduction in TEWL already after 1 or 2 months of treatment (bas/1 month t-test = 0.035, average value after 1 month = 9.05; bas/2 months t-test = 0.003 average value after 2 months = 8.77).

The values relative to the erythema index (Fig.3) of the skin recorded at the end of the treatment, remain unchanged.

The values relative to brightness (Fig.4) recorded in the first group revealed a increase of 0.47%, which was not statistically significant at the end of the treatment (t-test = 0.766) going from a basal average value of 65.29 to a final average value of 65.6). Similar results were obtained in the second group of volunteers, who had an L* parameter increased by 1.94% which was not statistically significant (t-test = 0.6618).

The sebum values (Fig.5) were significantly decreased by 30.92% (t-test = 0.0001) after 3
months of treatment (basal average value = 108.36, final average value = 74.86) in the first group of volunteers. Nevertheless, significant reductions were also recorded after one and two months of treatment (t-test = 0.003; t-Test = 0.0001).

The same results were obtained in the second group of volunteers with highly statistically significant decrease (t-test = 0.0001) at the end of treatment. There were also significant reductions of sebum in intermediate measurements (bas/1 week t-Test = 0.005; bas/1 month = 0.004; bas/2 months t-test = 0.0001).

Values of deep furrows (Fig.6) recorded in the first group after 3 months of treatment indicated a statistically significant reduction of 5.25% (t-test = 0.003), of the depth of the acne-related lesions going from a basal average value of 103.56 to a final average value of 98.11. As for the surface microrelief (Fig. 7), a statistically significant decrease was recorded equal to 1.18% (t-test = 0.003), going from basal average values of 50.14 to final average values of 49.55 at the end of treatment.

Significant variations in deep furrows and microrelief were also recorded in the volunteers who had used both the topical and oral products. Deep furrows measurements (Fig.6) after 3 months of treatment decreased, a statistically significant finding (t-test = 0.003), going from a basal average value of 104.17 to a final average value of 102.35. Measurements of variations in microrelief (Fig.7) showed a statistically significa-cant reduction (t-test = 0.0287), going from basal average values of 42.62 to final average values of 41.39 at the end of the treatment.

In Fig. 8 (a- b) and Fig. 9 (a- b) it is possible to observe the clinical acne improvement in two
patients representing the two different groups (topical treatment and topical plus oral placebo). Two volunteers dropped out of the study after 10 days of treatment because we observed the presence of slight erythema.

**DISCUSSION**

Both topical anti-acne cream and topical anti-acne plus placebo had a positive therapeutic effect on acne after the evaluated 90 days of application.

Recent studies showed the effectiveness of natural active principles present in this acne treatment (18). Lauric acid and standardised lipophilic extract of Serenoa repens are able to oppose the excessive production of sebum by the pilosebaceous unit. In particular, the standardised lipophilic extract of Serenoa repens inhibits the 5-reductase which is involved in testosterone metabolism and response for a series of androgen-mediated disturbances such as acne and greasy skin.

Standardized lipophilic extract of Krameria trianda Ruiz re-establishes the normal flora by preventing the proliferation of the microorganisms such as Propionibacterium acnes, Streptococcus pyogenes or Staphylococcus aureus, present in acne lesions (19, 20). Moreover the astringency of extract of Krameria trianda was mainly due to proanthocyanidins that have been isolated from this rhodan-root.

The 18-á glycyrrhetic acid in phytosome form and standardised lipophilic extract of Serenoa repens, determine an effective local anti-inflammatory response (21, 22).

In particular, the mechanism of action of 18-á glycyrrhetic acid is apparently due to its inhibition of 11-á-hydroxy-steroid dehydrogenase, an enzyme that reduces the activity of endogenous cortisol produced in response to the release of inflammation mediators. The standardized lipophilic extract of Serenoa repens inhibits the cyclo-oxidase, an enzyme involved in local inflammation and responsible for the release of some inflammation mediators.

Centella asiatica stimulates the production of collagen and correct tissue cicatrization (23). Centella’s active substances are called its “triterpenic fraction”. By interacting with fibroblasts, their main target, they accelerate the uptake and metabolism of lysine and proline (two amino acids need for the final structure of collagen), increase the synthesis and release of tropocollagen and stimulate the turnover of acid mucopolysaccharides in connective tissue. The statistical analysis of data in this clinical trial indicate an improvement of acne.
In fact, overall acne severity was significantly reduced in both groups: the improvement was recorded both on inflamed and non inflamed lesions.

The product tested produce a hydrating effect reducing dryness of the stratum corneum, thereby inducing improved functioning of the skin barrier expressed by the reduction in TEWL, as well as decreasing the production of sebum in subjects with acne lesions of varying severity and finally are effective in smoothing the skin, notably decreasing the anti-esthetic scars.

The erythema index recorded showed a modest, although significant erythematogenic effect of the products tested. In fact we must recall that two volunteers dropped out of the study after 10 days of treatment following a slight erythema. However a moderate burning sensation that was reported by some volunteers at the beginning of the study, decreased or disappeared during the treatment.

In conclusion, satisfying results were obtained at the end of two treatments (topical treatment, and topical + oral placebo), underlying the role of this topical plant complex treatment in improving acne lesions.
References


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