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A Randomized Controlled Study of a Novel Botanical Acne Spot Treatment

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ABSTRACT

OBJECTIVE: The study evaluated the tolerability and efficacy of a new presented treatment for acne. The product is an OTC topical gel consisting of 2% SA, which is also enriched in botanicals that have been shown to have anti-inflammatory properties.

DESIGN: The study was designed as a single-site, randomized, investigator-blinded, split-face 10-day study.

SETTING: Subjects enrolled with a minimum of 2 inflammatory papular acne lesions and 2 non-inflammatory open or closed comedones on both sides of the face in symmetrical locations, to the greatest degree possible. One side of each subject's face was randomly selected to receive the study treatment product.

PARTICIPANTS: 25 subjects, 15 female and 10 males, ages 12 to 43 years, suffering from mild to moderate acne.

Measurements: Study duration was 10 days, with study visits occurring at baseline (day 0), day 1, day 2, day 3, day 7, and day 10. Subjects underwent investigator facial evaluation and lesion assessment by dermatologist at each of the visit days. For the inflammatory lesions, the assessed parameters were erythema, elevation, induration, and overall impression. The assessed non-inflammatory parameters were elevation and overall impression.

Results: The observed difference between the treatment and the control group increased between day 1 and day 2 and reached an average of 15% to 20% with small varieties between the parameters and stayed similar across the remaining visits. Statistically significance (P less than 0.005) was achieved for all inflammatory and non-inflammatory tested parameters.

Conclusion: This study was performed to determine the safety, efficacy, and ease of use of a botanical acne treatment gel in providing a reduction in inflammatory acne lesion erythema, elevation, and induration. Erythema and elevation were the most influential parameters in inflammatory lesion with improvement noted after 2 days of application.

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INTRODUCTION

Acne is a common dermatologic condition occurring in more than 80% of adolescents age 13 to 18 years with varying severity. Acne prevalence is increasing in young adults older than 25 years, specifically women.[1-2] Over the counter (OTC) topical therapy is based on the monographed ingredients benzoyl peroxide (BPO), and salicylic acid (SA). BPO is effective in concentrations ranging from 2.5% to 10% with an antibacterial and

comedolytic activity. BPO is poorly tolerated, with the most common side effects being concentration-dependent skin irritation and allergic contact dermatitis. SA functions as a keratolytic agent and is administered topically at concentrations equal and below 2% and functions as an anti-inflammatory. BPO and SA are both effective in reducing lesion counts, however, rapid inflammation and redness reduction is not present in the OTC market.[3-6]The use of botanicals, as part of alternative or complementary acne treatment, is still not widely available.[7-8] In this study we present a new botanical based anti-inflammatory acne treatment that was found to be effective and well tolerated in improving the acne symptoms. An OTC acne treatment (Kamedis Acne Spot Treatment, Kamedis Ltd., Tel-Aviv, Israel), topical gel product consisting of 2% SA and botanicals was studied. The spot treatment is based on herbal botanical ingredients that have been shown to have anti-inflammatory, anti-bacterial, anti-oxidative activity as well as reduction is sebum secretion.[9-21] This study was designed to evaluate the tolerability and efficacy of the new presented treatment for acne.

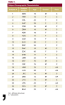
METHODS

25 subjects, 15 females and 10 males, ages 12 to 43 years, with mild to moderate acne were recruited and qualified for the study. The study was designed as a single-site, investigator-blinded, split-face 10-day study (Dermatology Consulting Services, PLLC, High Point, NC). The study was conducted under Institutional Review Board (Concordia IRB, Beach Haven, NJ), a signed informed consent form and a photographic release form were obtained from each subject prior to performing any study procedure.

Subjects enrolled according to the inclusion criteria with a minimum of 2 inflammatory papular acne lesions and 2 non-inflammatory open or closed comedones on both sides of the face in symmetrical locations, to the greatest degree possible. Subjects did not use any topical acne treatments for 2 weeks prior to study entry, did not take any oral acne medications for 4 weeks prior to study entry, and did not use any topical acne medications for 2 weeks prior to study entry.In the study, one side of each subject's face was randomly selected to receive the study treatment product. The treatment selected side of the face was washed pre-treatment by Dove sensitive skin unscented soap bar and was treated by Kamedis spot treatment. Subjects were requested to apply the treatment product three times daily following face wash with the Dove bar, as per instructions, morning noon and evening. The non-treated face side or the control side was washed by the Dove bar three times daily, as the treatment side, however was not treated with a topical product.The study duration was 10 days, with study visits occurring at baseline (day 0), day1, day 2, day 3, day 7, and day 10. Subjects underwent investigator facial evaluation and lesion assessment by dermatologist at each of the visit days. Digital photos were taken of the face at day 0, day 1, day 2, day 3, and day 10. Images were taken 90 degrees, +45 degrees, and -45 degrees to the subject with a Nikon D-90 camera in a Canfield 3-point head mount with an IntelliFlash system and a consistent f-stop for reproducibility at all time points.The investigator assessed each inflammatory and non-inflammatory lesion on each side of the face separately for a number of parameters at each of the visit days 0, 1, 2, 3, 7, and 10. For the inflammatory lesions, the assessed parameters were erythema, elevation, induration and overall impression. As for the non-inflammatory, the assessed parameters were elevation and overall impression. Per each parameter, the following grading scale was used: 0=None, 1=Minimal, 2=Mild, 3=Moderate, and 4=Severe.Following the treatment, on day 10, the subjects completed a sponsor-supplied marketing questionnaire and provided their comments for the entire experience.The statistical analysis used a two-way analysis of variance (ANOVA) with visit and treatment/control as main factors and the interaction between them. A significant interaction would mean that the difference between the treatment and the control is not similar across visits. Factors with P-Values smaller than 0.05 are considered as statistically significant. For each parameter, the original scores have been transformed to percentage of improvement by calculating the percentage of increased score comparing to the score measurement of each patient at baseline (day 0).

RESULTS

Out of the 25 subjects enrolled, 24 subjects completed the study. One subject did not complete the study due to personal reasons unrelated to the tested product. No adverse experiences or events occurred during the trial.Demographic characteristics of the subjects are presented (Table 1). No significant statistical difference was observed in characteristics between the randomly selected treatment and control lesion groups in the baseline visit (day 0).The investigator assessed at each visit the subject inflammatory chosen lesions for



erythema (Figure 1), elevation (Figure 2), induration, and overall impression (Figure 3),

and the non-inflammatory lesions for elevation and overall impression.In general, the Kamedis Acne Spot Treatment demonstrated a consistent improvement over the control group. Improvement is observed after one day of treatment and continues to expand over the control after the following day (day 2). Kamedis Acne Spot Treatment maintains its advantage during the following visits up to day 10. The observed difference between the treatment and the control group increases between day 1 and day 2 and reaches an average of 15% to 20% with small varieties between the parameters and usually stays similar across the remaining visits. Statistically significance ($P<0.005$) was achieved for all inflammatory and non-inflammatory tested parameters.The erythema improvement measured on inflammatory lesions reached around 20% difference between the tested product and the control after 2 days and achieved the maximum difference of 24% on day 3. The erythema improvement magnitude of the tested product reached 50% after 10 treatment days, keeping a similar difference values between the tested product and the control (Figure 1).The elevation improvement that was measured on the inflammatory lesions only, reached 18% of improvement on the first day, this was also the difference comparing to the control, since the control value showed 0% on the first day. On the second day the difference was over 20% and kept similar or greater difference until day 10. The elevation improvement magnitude of the tested product reached 63% on day 10 (Figure 2).The induration improvement on inflammatory lesions showed smaller difference comparing to the two previous parameters. On day 2, the difference between the tested product and the control reached 10% and increased to 20% on day 3, keeping similar difference for the rest of the study. The induration improvement magnitude of the tested product reached 52% by day 10.The overall impression of the inflammatory lesions of the tested product reached 66% by day 10, keeping a 20% difference from the control starting from day 2 and 3 (Figure 3).The elevation improvement of the tested product that was tested on the non-inflammatory lesions showed smaller value of improvement by day 10 (31%) comparing to the inflammatory lesions. The difference between the tested product and the control was smaller as well, starting with 5% on day 2 and increased to 13% on days 7 and 10.The overall improvement of the non-inflammatory lesions was very similar to the elevation results, starting with 7% difference between the tested product and the control on day 2 and reached 13% of difference on day 10, with 31% as final magnitude of the improvement of the tested product by day 10.In addition to the measured parameters, clear improvement was visually evident as early as in day 2 or 5 applications of the treatment product (Figure 4a and 4b).

DISCUSSION

The presented study evaluated a new botanical based acne treatment with anti-inflammatory activity. The product was found to be effective and well tolerated in improving the acne symptoms. The control side included a general wash by a soap, however did not include a topical treatment for the inflammatory and non-inflammatory acne lesions. The control is a challenge in acne studies because healing occurs without intervention. On inflammatory lesions, the acne study botanical demonstrated better results over time, usually after two days except for elevation in which significant improvement is evident after one day of treatment. On non-inflammatory lesions, the acne study botanical was still better over the control although with a smaller magnitude than the ones observed in the inflammatory lesions.The acne study investigated a product that was based on 10% herbal botanical ingredients with anti-

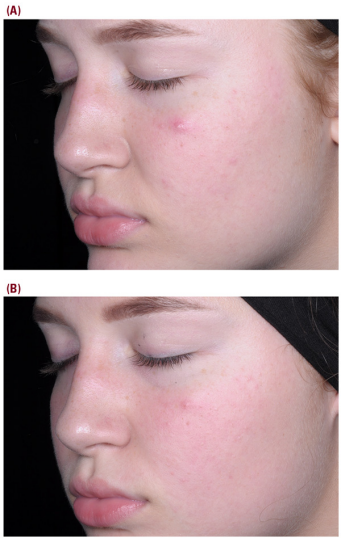


FIGURE 4. Visual improvement after 2 days, 5 applications. (A) Day 0, (B) Day 2.

inflammatory and anti-bacterial activity such as the Rheum Palmatum, Portulaca Oleracea, Chrysanthemum Indicum, Scutellaria baicalensis, Phellodendron Amurense, Sanguisorba Officinalis, and Sapindus Mukorossi. The Rheum Palmatum and Scutellaria baicalensis also show anti-oxidative activity as well as reduction is sebum secretion, which may assist in improving and relieving the severity of acne lesions. The botanicals were selected due to their anti-inflammatory properties.[9-17] They were chosen out of hundreds of herbs due to thorough literature review that was followed by in vitro studies on artificial skin model. The in vitro tests studied the anti-inflammatory activity of the botanicals by the inhibition of the TNF alpha release, and yielded promising results in the combination of the above herbs. The chemical active molecules that are connected with the anti-inflammatory mechanism of the rheum palmatum are Emodin and Aloe-Emodin.[18-20] Both are being produced by the rheum palmatum herb and are effective and selective inhibitors of the enzyme 11β-HSD1, which catalyzes the conversion of the stress hormone cortisol to the inactive metabolite cortisone. Moreover, updated scientific evidence supporting the use of emodin in medicine for the treatment of various inflammatory diseases through the regulation of inflammasome activation. Emodin attenuated NLRP3 inflammasome activation, leading to decreased secretion of cleaved IL-1β and blocking of the inflammasome-induced pyroptosis.[21]This study is a pilot preliminary study presenting this original product, and therefore included a small sample size, which is the main shortcoming of the study.

SUMMARY

This study was performed to determine the safety, efficacy, and ease of use of a botanical acne treatment gel in providing a reduction in inflammatory acne lesion erythema, elevation, and induration. Erythema and elevation were the most influential parameters in inflammatory lesion with improvement noted after 2 days of application.

DISCLOSURES

This study was wholly funded by Kamedis Ltd. Deganit Barak-Shinar is an employee of Kamedis Ltd. the manufacturer of the Kamedis Acne Spot Treatment as well as the sponsor of this study. Zoe Diana Draelos received an unrestricted educational grant from Kamedis to conduct the research detailed in this manuscript.

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