

SHORT REPORT

A skincare combined with combination of adapalene and benzoyl peroxide provides a significant adjunctive efficacy and local tolerance benefit in adult women with mild acne

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Abstract

Introduction Acne in adult women is an increasing reason for dermatological consultations.

Objective The aim of this study was to assess in adult women with mild acne the efficacy and tolerance of a daily adjunctive application of a skincare (Normaderm[®], Laboratoires Vichy, France) to a fixed combination of adapalene/benzoyl peroxide daily or every other evening and a standard emollient.

Methods Subjects were randomized to receive the fixed combination applied either every evening or every other evening and a daily application of the standard emollient and the test care or a once daily application of the fixed combination and the standard emollient alone. Clinical evaluations at Day 0, Day 45 and Day 90 included the count of acne lesions, assessment of clinical improvement and local tolerance. The quantitative lipid profile of the stratum corneum of the forehead was also determined.

Results After 90 days of application, acne had improved in all 299 subjects with a statistically significant difference in favour of the test care regimens ($P < 0.05$). Moreover, skin quality, subject satisfaction, skin discomfort and sebum composition were in favour of these regimens.

Conclusion In conclusion, the tested skincare combined with a fixed adapalene and benzoyl peroxide combination provides a significant adjunctive efficacy and local tolerance benefit in adult women with mild acne.

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Conflicts of interest

None declared.

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Introduction

Acne in adult women is an increasing reason for dermatological consultations.^{1,2} A combination of benzoyl peroxide and topical retinoids is proposed in the recent guidelines as the first-line treatment in women with acne.^{3–6}

A specific skincare (Normaderm[®] anti-imperfections care, Laboratoires Vichy, Asnières, France, hereafter ‘the test care’) has been developed associating phenylethyl resorcinol (Phe-resorcinol), a skin depigmenting and antipigmenting agent

and lipohydroxy acid (LHA), a salicylic acid derivate, targeting the corneodesmosome, stimulating cell renewal in the upper skin layers and reducing pigmentation. Both have antibacterial properties against *Propionibacterium acnes*.^{7–12} Moreover, it contains capryloyl glycine and salicylic acid combined with the patented Airlicium[™] Technology, which absorbs sebum and sweat.

This study assessed its efficacy and tolerance as an adjunctive skincare to a fixed adapalene and benzoyl peroxide combination in adult women with mild acne.

Methods

A prospective, randomized study was conducted in Spain and Poland in compliance with local regulatory and ethical requirements. Three hundred healthy women between 25 and 35 years with mild acne, of any phototype, with no topical acne treatment within the two previous weeks, no oral acne treatment within the four previous weeks for antibiotics or 6 months for isotretinoin and no other face dermatoses were recruited. All women who provided written consent and met the inclusion criteria were randomized at each study site in a 1 : 1 : 1 way to receive for 90 days:

- a standard non-comedogenic emollient (containing water, glycerine, cyclohexasiloxane, stearic acid, butylene glycol, Cosmetique Active, Asnières, France) in the morning and in the evening a fixed adapalene 0.1% and benzoyl peroxide 2.5% combination (Epiduo®; Galderma Laboratories, La Défense, France), hereafter Group A, or
- the test care and the standard emollient in the morning and in every other evening the fixed combination, hereafter Group B, or
- the test care and the emollient in the morning and in the evening the fixed combination, hereafter Group C.

Table 1 summarizes treatment regimens.

Investigators were not aware of the regimens to which subjects were randomized. Products were provided in neutral cardboard boxes with an instruction leaflet on how to apply the products.

The primary evaluation endpoint was the mean acne lesion count after 90 days. Clinical evaluations at Day 0, 45 and 90 included the count of papules, pustules, nodules and inflammatory cysts, as well as of open and closed comedones. Local tolerance was assessed at Day 45 and 90. At all visits, the investigator also assessed the global clinical improvement on a 7-point scale ranging from worsening to complete clearance and the overall skin aspect (seborrhoea, erythema, dilated pores, dull and irregular complexion, postinflammatory hyperpigmentation) and the tolerance (discomfort and stinging) on a scale from 0 (none) to 9 (very high). At Day 90, the investigators and subjects rated the skin care regimens globally.

The quantitative lipid profile of the *stratum corneum* of the forehead of selected subjects (24 subjects planned in each group)

Table 1 Treatment groups regimens

	Group A	Group B	Group C
Every morning	Standard emollient	Normaderm® + Standard emollient	
Evening	Every evening Fixed combination adapalene/benzoyl peroxide	Every other evening Fixed combination adapalene/ benzoyl peroxide	Every evening Fixed combination adapalene/benzoyl peroxide

was determined at Day 0 and 90 throughout specific lipid markers – squalene, sterols, free fatty acids, waxes, glycerides and total neutral lipids using a non-invasive, solvent-free method (Synelvia, Labège, France).

The 'R' software (Foundation for Statistical Computing, Vienna, Austria 2012) was used for statistical analysis. The Student t-test was used to compare mean differences between Day 90 and Day 0, of investigator and subject assessments. The Mann–Whitney test was used to compare the distribution of lipid variables between groups; the Wilcoxon test was used for the intragroup comparison. Probability limits were set at 5% using a two-tailed approach.

Results

In total, 299 subjects completed the study: 99 in Group A and 100 in both Group B and in Group C. One subject in Group A was lost to follow-up.

At Day 0, demographic (median age 29 years (24–36) in Group A, 30 years (24–36) in groups B and C), clinical and cutaneous lipid characteristics were similar for all three groups.

All regimens significantly reduced ($P < 0.05$) acne lesion counts as early as Day 45, with a sustaining effect at Day 90. At both visits, the difference between Groups B and C compared to Group A was significant ($P < 0.05$) for papules and pustules (Fig. 1).

Global clinical improvement at Day 45 and 90 was significantly higher ($P < 0.05$) for subjects in Group B (48% and 85%) and C (46% and 82%), compared to those in Group A (24% and 62%) with no statistically significant difference between Group B and C.

After 90 days and according to the investigators, the skin aspect had significantly improved ($P < 0.05$) in all groups, with a significant difference between Group B and C vs. Group A (Fig. 2).

Subject satisfaction at Day 90 was significantly higher ($P < 0.05$) in Groups B (96%) and C (93%) compared to Group A (88%).

Safety/Tolerance

No subject withdrew from the study for any tolerance or safety issues and no adverse events were reported.

Tolerance was rated 'good to excellent' in 97% of the subjects in Group B and in 88% of subjects in Group C. Conversely, the investigators rated the tolerance of the standard association of the fixed combination and the standard emollient (Group A) good to excellent in only 84% of the subjects. Differences were significant ($P < 0.05$) for Group B and C vs. Group A and for Group B vs. Group C.

Discomfort had improved in subjects in groups B and C applying the test anti-imperfection care adjunctively compared to subjects applying the standard emollient only ($P < 0.05$) (Fig. 2).

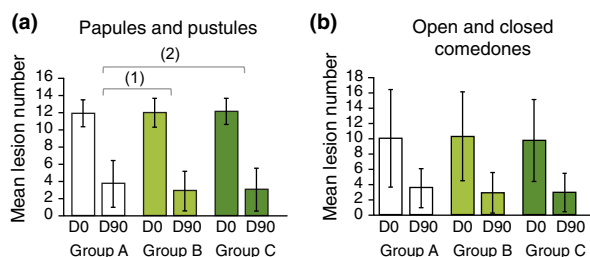


Figure 1 Mean acne lesion count at Day 0 and Day 90. Differences were statistically significant at Day 90 from Day 0 for all treatment groups. The difference was statistically in favour at Day 90 for Group B (1) and C (2) compared to Group A for papules and pustules ($P < 0.05$). Mean papules and pustules counts at D0: 11.94 for Group A, 12.04 for Group B, 12.18 for Group C. Mean papules and pustules counts at D90: 3.76 for Group A, 2.93 for Group B, 3.07 for Group C. Mean of the deltas D90 vs. D0 are -8.18 for Group A, -9.11 for Group B, -9.11 for Group C.

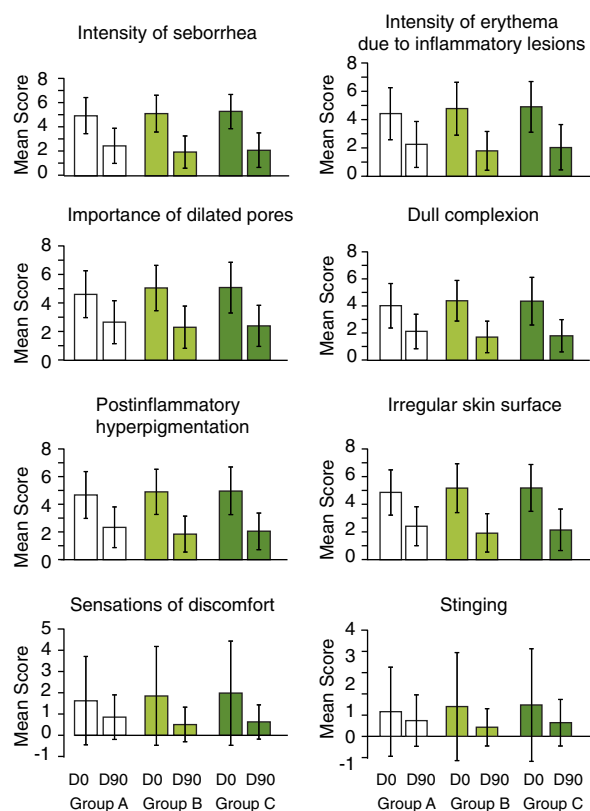


Figure 2 Skin aspect, discomfort and stinging at Day 0 and Day 90. At Day 90, all investigated items had significantly improved from Day 0 in all groups ($P < 0.05$). Differences between Group B and C vs. Group A at Day 90 were significant for all items.

Quantitative characterization of the lipid profile

A total of 70 complete skin lipid profiles (23 from Group A, 23 from Group B and 24 from Group C) were available for quantitative skin lipid assessment.

At Day 90, the lipid profile had significantly improved for all subjects. However, compared to skin samples from Group A, the quantity of the following compounds of samples from Group B and C had significantly improved: free fatty acids (-16% vs. -30% and -29% , respectively for Group A, B and C), squalene (-19% for Group A vs. -30% for both groups B and C) and reserve forms (1% vs. 13% for both groups B and C). The difference between Group B and Group A was significant for glycerides (-21% vs. -15% , respectively) and oxidized squalene (SQOOH, -37% vs. -28% , respectively). Differences in favour of Group C compared to Group A were almost significant for glycerides (-20% vs. -15%). Detailed mean results at Day 0 and 90 are provided in Fig. 3.

Discussion and conclusion

Adding the test care containing Phe-resorcinol, LHA and Aircium[®] to a fixed combination of adapalene and benzoyl peroxide improved significantly acne as well as seborrhoea, erythema, pores, dull complexion, irregular complexion, discomfort and local tolerance.

Interestingly, the improvement was significantly higher with regimens comprising the test care, not only when the fixed combination was applied daily (Group C) but also when this combination was applied every other evening (Group B). This is of special interest, as recent guidelines confirm the daily use of a combination of topical retinoid and benzoyl peroxide in the evening and if needed an emollient in the morning to reduce potential local side-effects frequently observed with retinoids and benzoyl peroxide.^{4,5} The present results show that, despite these recommendations, a once-every-other-day application of a fixed combination, commonly used by clinicians especially during the initiation of treatment provides in association with daily adjunctive use of the test care similar results to the once daily application of a fixed combination with no difference in efficacy. This could be related to the fact that the test care decreases the alterations of barrier that fixed combination induces and help restore microbiote, lipidic film and stratum corneum. In addition, less irritation and less alteration of skin barrier, decrease the activation of innate immunity with the production of the comedogenic IL-1 by keratinocytes, thus participating to the decrease in acne lesions.

Squalene and waxes are characteristic compounds of sebaceous glands lipids while sterols are components of the epidermal lipids. In acne, qualitative and quantitative sebum modifications throughout increased sebum secretion increased squalene/oxidized squalene and increased free fatty acids have

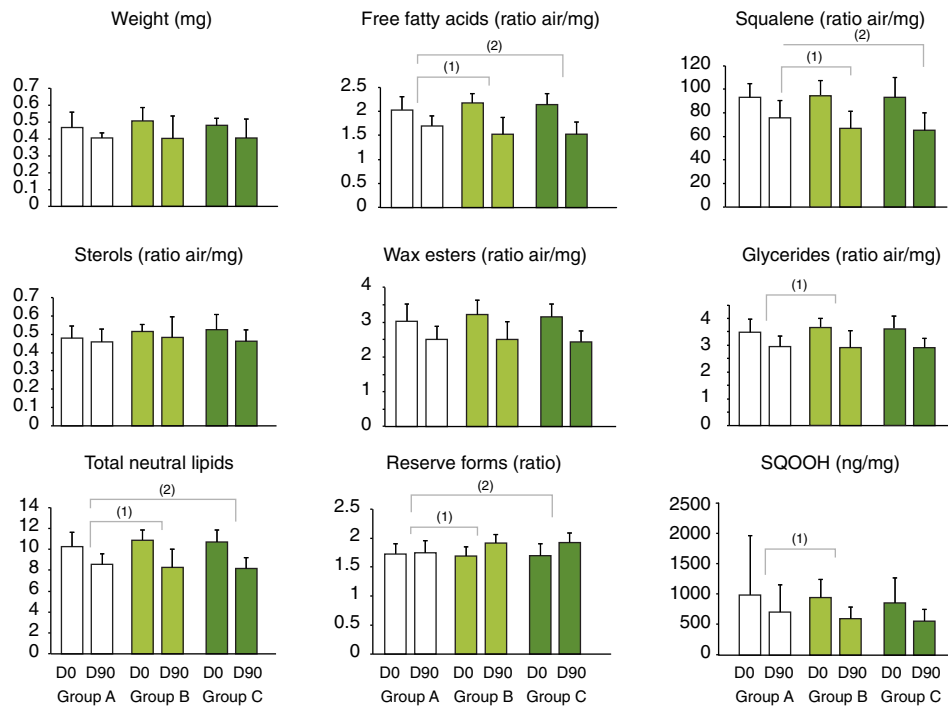


Figure 3 Modifications of lipid compounds at Day 90 compared to Day 0. The differences between Group B (1) and Group C (2) were significant ($P < 0.05$) compared to Group A. SQOOH, oxidized squalene.

been observed.¹³ In addition, squalene oxidation has been identified as a marker of environmental pollution.¹⁴ The quantitative lipid analysis confirmed that the test care applied adjunctively for 90 days to a fixed combination and a standard emollient significantly ($P < 0.05$) improved and equilibrated the quantitative composition of the sebum in patients with mild acne. Moreover, the decreased quantity of waxes and glycerides may indicate a better moisturized and protected skin via a higher filmogen activity while the observed decrease in oxidized squalene suggests a decreased *P. acnes* activity and a protection against negative environmental factors.¹⁴

Results of this study show that the skin barrier function might have improved after 90 days of daily application of the test care adjunctively to the fixed combination and a standard emollient. This improvement may be potentially due to the fact that the test care improved the free fatty acid profile while it rebalanced the profile of reserve forms playing a role in the improved skin discomfort. No such improvement was observed with the standard emollient alone.

In conclusion, Normaderm[®] care containing Phe-resorcinol, LHA and Airlcium[®] combined with a fixed adapalene and benzoyl peroxide combination provides a significant adjunctive efficacy and local tolerance benefit in adult women with mild acne.

It may enable the use of the adapalene and benzoyl peroxide combination once every other day.

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