Improved Reduction in Propionibacterium acnes Counts with a Novel 2.5% Benzoyl Peroxide Formulation Compared to a 2.5% Benzoyl Peroxide

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INTRODUCTION

- The gram positive anaerobic bacterium, Propionibacterium acnes *(P. acnes)*, has been implicated in the pathogenesis of acne.
- Benzoyl peroxide *(BPO)* has been shown to have potent anti-*P. acnes* effects in humans.
- The effect of BPO appears to be rapid, showing significant reductions in both surface and follicular *P. acnes* within 2-3 days after application.
- Prior recommendations from the Federal Register, 21 CFR Part 333, define a standard of reduction of *P. acnes* counts of 0.75 log by the active ingredient, and a reduction of *P. acnes* counts of at least 0.75 log relative to baseline.

STUDY DESIGN AND METHODS

Objective

- To compare a prototype benzoyl peroxide 2.5% formulation *(BPO)* and a marketed BPO 2.5% *(Proactiv®)* formulation on:
  - Time required to reduce surface and follicular *P. acnes* after a single application.
  - Duration of activity after a single application.

Design and Methods

- 3-day, split-face, randomized study of 10 subjects.
  - Baseline sampling included a bacteriological scrub on the forehead and right and left cheeks, and cyanoacrylate follicular biopsies on the right and left forehead *(see Fig. 1 and 2)*.
  - Biopsies were also taken from each side of the face at baseline and 3 and 8 hr post-treatment.
- From the follicular biopsies, 20 of the largest plugs from the cyanoacrylate cast were analyzed. The 20 plugs were randomly selected across the whole cast surface using a microscope and visible light source.
  - Further bacteriological samples were collected from each side on an adjacent area at 3, 8, 24, 48, and 72 hours *(hr)*.
    - For all samples, the density of *P. acnes* was expressed as log10 cfu(s) per square centimeter *(cm2)*.
  - Controlled amounts of each treatment were applied by a technician to one side of each subject's face. The central area of the face did not receive any treatment. The side on which the prototype formulation was placed was counterbalanced across subjects.

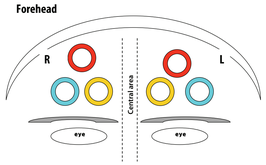

Figure 1

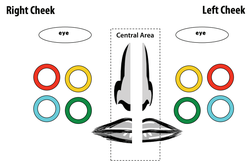

Figure 2

Patient Eligibility

Inclusion criteria

- Males/females at least 12 years of age.
- Mild to strong *(grades 1-3 on a 0 = none to 3 = strong)* porphyrin fluorescence uniformly distributed across the entire forehead and cheeks during a screening examination.
- No use of facial products or exposure to sunlight during study period.

Exclusion criteria

- Allergy to benzoyl peroxide.
- Papulo-pustular rosacea and other skin diseases on the face (except minor acne) or skin conditions that could interfere with study results.
- Sunburn, make-up or beard.
- Use of the following medications within the described period.
  - Medicated facial cleansers including antibacterial soaps, topical AHAs, and anti-acne medications (BPO, retinoids, antibiotics) – 2 weeks
  - Topical retinoids – 4 weeks
  - Topical and systemic antibiotics – 4 weeks
  - Steroids – 4 weeks
  - Investigational drugs – 4 weeks
  - Systemic retinoids – 1 year
- Concurrent use of other medicated products on the face.
- Uncontrolled systemic disease, insulin-dependent diabetes or immunological disorders.

Efficacy Variables

Primary efficacy endpoints

- Reduction in *P. acnes* density *(as log10 cfu/cm2)* from baseline to 3 and 8 hr post-treatment, as determined by either follicular biopsies or by bacteriological scrubs on the forehead.
- Reduction in *P. acnes* density *(as log10 cfu/cm2)* from baseline to 24, 48 and 72 hr post-application, as determined by bacteriological scrubs on cheeks.

Data Analyses

- Densities of *P. acnes (as log10 cfu/cm2)* at baseline, and 3, 8, 24, 48, and 72 hr post-treatment, based on both the bacteriology scrub and the follicular biopsy for both right and left side of the forehead and the right and left cheeks are shown graphically.
- Within-treatment differences over time were assessed as change from baseline to each time point on the forehead as well as on the cheeks.

RESULTS

Demographics and baseline characteristics

Characteristic	N=10
Mean (SD) age	28.0 (12.8)
Percent female	80.0%
Percent Caucasian	90.0%

Efficacy

- Both the prototype 2.5% BPO solution and the marketed BPO product reduced the density of *P. acnes* at 3 and at 8 hours. The reduction in *P. acnes* was greater, however, for the prototype product than the marketed product *(see Figure 1)*.

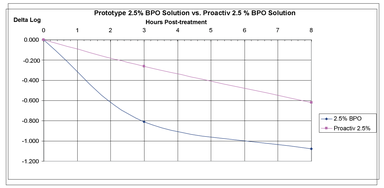

Fig. 1 Reduction in *P. acnes* bacteriological counts 3 and 8 hours after application of a prototype BPO 2.5 % solution and a marketed BPO 2.5% formulation, based on follicular biopsy.

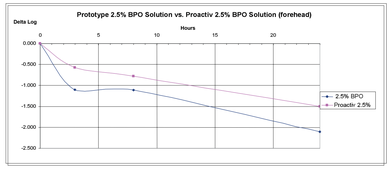

Fig. 2 Reduction in *P. acnes* bacteriological counts on the forehead up to 72 hours after application of a prototype BPO 2.5 % solution and a marketed BPO 2.5% formulation, based on the results of bacterial scrubs.

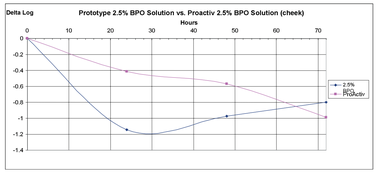

Fig. 3 Reduction in *P. acnes* bacteriological counts on the cheek up to 72 hours after application of a prototype BPO 2.5 % solution and a marketed BPO 2.5% formulation.

- Based on bacteriological scrubs, both treatments reduced *P. acnes* counts over the course of the study. The difference between treatments was less remarkable for the forehead *(Figure 2)* than for the cheeks *(Figure 3)*, which showed the greatest reduction at 24 and 48 hours. By 72 hrs, the curves for the two treatments had converged although both were still substantially lower than baseline.

CONCLUSIONS

- Benzoyl peroxide has been shown to have potent anti-*P. acnes* activity, making it an effective treatment for patients with acne.
- A number of formulations of BPO are available, but they may vary in the extent and time course of their effects.
- The results of this study suggest that the prototype BPO 2.5% formulation used in this study has substantially greater *in vivo* anti-bacterial activity than a currently marketed formulation, and that its effects persist for at least 72 hr even after only a single application.
- These findings imply that the prototype solution has greater penetration into the follicle.
  - Supporting this conclusion, data from a percutaneous absorption study *(Study OMP 05-05; on file)* demonstrated greater localization of BPO on and in the stratum corneum and in the epidermis after application of the prototype BPO 2.5% than the Proactiv BPO 2.5%.
- Further study is warranted to evaluate the effects of the novel solution on different types of acne lesions and for longer periods of time.

REFERENCES

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DISCLOSURES

This study was funded by OMP, Inc.