A COMPARISON OF PATTERNS OF DEPOSITION OF TWO FORMULATIONS OF BENZOYL PEROXIDE ON THE SKIN AND IN THE FOLLICULAR OSTIA AS VISUALIZED BY SCANNING ELECTRON MICROSCOPY

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INTRODUCTION

Benzoyl peroxide (BPO) can offer good efficacy in treating acne vulgaris as a consequence of both its bactericidal activity against *Propionibacterium acnes* and its comedolytic activity.[1,2] Nevertheless, physicochemical challenges in the formulation of BPO products mean that the bioavailability of BPO and its ability to enter follicles (and so act directly at the pathogenic source of acne) may be significantly compromised. For example, it is thought that only a very small proportion of available BPO molecules in commercially successful BPO formulations are actually delivered to the follicles. It is possible therefore that improving the bioavailability of BPO, and improving delivery to the follicles, could enhance the clinical efficacy of BPO still further.

A number of factors are believed to hinder the delivery of BPO to the follicles. First, BPO molecules are poorly soluble. Second, they aggregate into clusters that may be large enough to prevent them even entering the follicles—an evaluation of three commercially available BPO products showed that the BPO clusters in the formulations had diameters of 5-50 µm, 10-100 µm, and 50-100 µm, respectively,[3] whereas an average hair follicle has a diameter of approximately 50 µm. Clustering also inhibits the action of the BPO because most of the BPO molecules become trapped in the interior of a cluster, hindering their ability to interact with *P. acnes*. A third factor that can impact the delivery of BPO to the follicles is the vehicle—for example, BPO formulations may be oil in water emulsions and these do not readily flow into follicles.

In the past, attempts to use various solvents to improve the solubility of BPO were thwarted because increasing the solubility of BPO was found to negatively impact its stability.[4] However, more recently, a novel solubilized 5% BPO gel has been developed that is designed to deliver superior BPO solubility without any such stability problems. Based on the results of comparative trials,[5] the bioavailability of BPO in this novel solubilized BPO gel is thought to be substantially higher than that in other commercially available formulations. In addition, the vehicle is designed to allow the passage of BPO into the follicles.

To evaluate how this formulation behaves when applied to the skin, we have compared its pattern of deposition on the surface of the skin and in the follicular ostia with that of a commercially available generic 5% BPO gel. Clinical efficacy data have been reported elsewhere.[6,7]

METHODS

Treatment

- Two target areas on the face of a healthy volunteer were identified for treatment, one on the left side and one on the right side.
- Then, both sides of the subject's face were washed using a gentle skin cleanser.
- After waiting 30 minutes, a silicone elastomer replica was created of the skin surface in each of the right and left target areas.
- The face was cleansed again and a single application of the:
  - Novel solubilized 5% BPO gel was applied to one side of the face
  - Generic 5% BPO gel was applied to the other side of the face.
- After waiting 30 minutes, another silicone elastomer replica was created of the skin surface in each target area.

Scanning electron microscopy

- All replicas were negative images of the skin and were converted to positive replicas before viewing under a scanning electron microscope at a magnification of 300x.
- An independent expert who was experienced in analyzing electron microscopy images, and who was blinded as to both the type of treatments applied to the skin and their anticipated effects, evaluated each image and reported their observations.

RESULTS

- The pre-treatment skin replicas from both sides of the face showed:
  - No particulate matter on the surface of the skin or in the follicles
  - Superficial squamous cells that were intact and regular in appearance.
- After application of the generic BPO gel, a significant volume of residual material was clearly visible on the surface of intact squamous cells (Figure 1). There was no evidence of similar material in the follicular ostia.
- After application of the novel solubilized BPO gel, no visible residue was apparent on the skin surface (Figure 2) but globular material was evident in the follicular ostia. This suggests that the gel was entering the follicles.

CONCLUSIONS

The results of this study suggest that the novel solubilized BPO gel becomes distributed evenly over the surface of the skin, with BPO able to enter the follicles and so provide anti-acne efficacy directly in the interior of the follicles (where the pathogenesis of acne is focused) as well as on the skin's surface. In contrast, the generic BPO gel does not appear to be distributed evenly on the skin and leaves behind a residue that is visible under the microscope. No follicular penetration of this formulation was evident.

Although these findings are limited to that from a single exposure in one subject, the results of a study in 24 healthy volunteers support the hypothesis that the novel solubilized BPO gel penetrates the follicles—the intrafollicular bactericidal activity was greater with the novel solubilized 5% BPO gel than with either a prescription generic 5% BPO gel or a prescription 5% BPO/antibiotic combination product.[5] Furthermore, in a study of 34 patients with mild to moderate acne vulgaris, twice-daily applications of the novel solubilized 5% BPO gel in conjunction with a salicylic acid-based toner resulted in a greater reduction in the non-inflammatory lesion count than twice-daily applications of a prescription 5% benzoyl peroxide/antibiotic product (34% vs. 21% after 2 weeks). In addition, both treatments achieved comparable reductions in the inflammatory lesion count (52% vs. 50% after 2 weeks) even though the combination product had the presumed advantage of containing an antibiotic in addition to the benzoyl peroxide.[6]

FIGURE 1 After treatment with the generic BPO gel, residue (in the form of both individual particles and a more porous coating) is evident on the surface of the skin (magnification 300x).

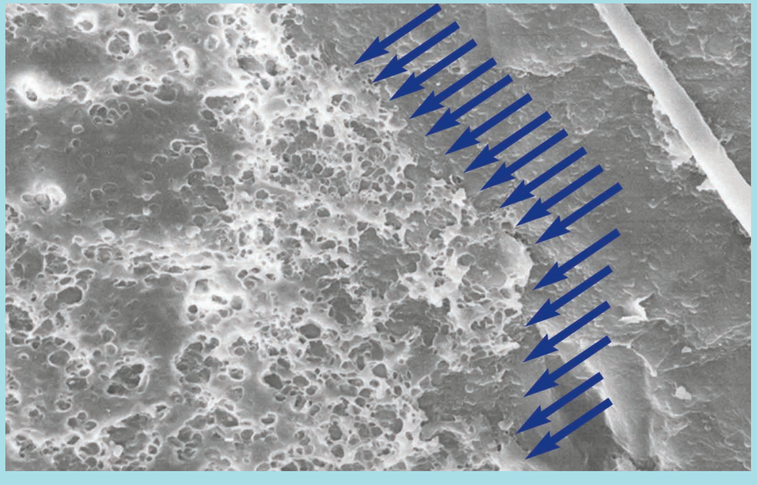
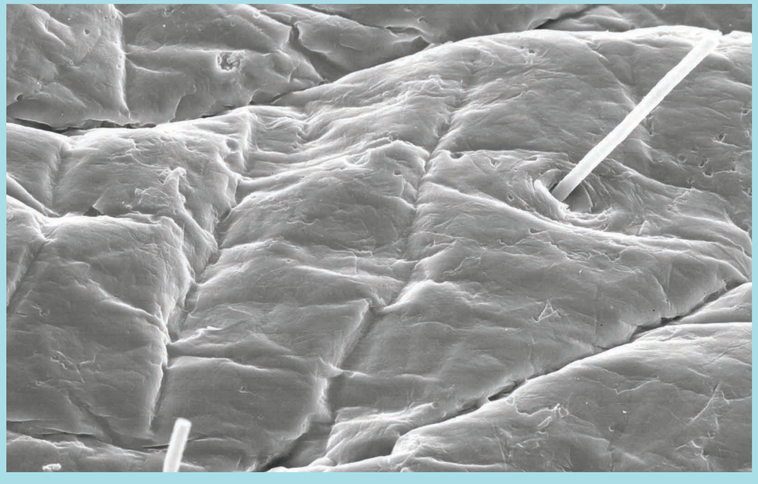


FIGURE 2 After treatment with the novel solubilized BPO gel, the gel appears to have been distributed evenly across the skin's surface and to have entered some follicles (magnification 300x).



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DISCLOSURES

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