Interaction of Topical Sulfacetamide and Topical Dapsone With Benzoyl Peroxide

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Background: A recent study demonstrated evidence of a yellow-orange discoloration of the skin and hair when topical dapsone gel was combined with benzoyl peroxide. This phenomenon had previously been observed by one of us (A.B.F.) when sulfasalazine was combined with benzoyl peroxide. To investigate these interaction phenomena, topical dapsone gel and sulfacetamide sodium lotion were combined with various topical acne treatments, including benzoyl peroxides, clindamycin phosphate, and retinoids.

Observations: Products containing benzoyl peroxide produced an orange-brown discoloration when mixed with either sulfacetamide or dapsone.

Conclusions: Knowledge of the chemical reaction between benzoyl peroxide and sulfacetamide and dapsone will help minimize the occurrence of this interaction on our patients' skin.

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Finally, the napkin was washed and dried with a nonbleach detergent in a warm/cold cycle to determine whether the product residue was easily removable. All photographs are original, without color correction, but were taken in a room with natural and fluorescent lighting, which varied over the course of the day.

RESULTS

In all groups containing sulfacetamide, including the control, a faint orange ring was visible at 30 minutes and remained at 12 hours (Figure 2). A yellow tint was present in the sulfacetamide plus benzoyl peroxide group at 3 hours, followed by a similar yellow tint in both sulfacetamide plus benzoyl peroxide and clindamycin plus benzoyl peroxide groups at 4 hours. These yellow tints gradually developed into an orange-brown color by 12 hours. Aside from the faint orange ring, there was no color change in the sulfacetamide control or in the sulfacetamide plus clindamycin, sulfacetamide plus tretinoin, sulfacetamide plus tazarotene, or sulfacetamide plus adapalene groups.

In the groups containing dapsone gel, an orange change occurred in the dapsone gel plus benzoyl peroxide group at 1 hour, followed by both dapsone plus clindamycin and dapsone plus benzoyl peroxide groups at around 2 hours. At 6 hours, these 3 groups were brown. A faint yellow color change was noted in the dapsone gel control, dapsone gel plus clindamycin, dapsone gel plus tretinoin, dapsone gel plus tazarotene, and dapsone gel plus adapalene groups at 5 hours; it persisted for 12 hours. After the napkin was washed and dried, no product remained in any of the groups containing sulfacetamide. In the dapsone gel–containing groups—the dapsone plus benzoyl peroxide and the 2 combination dapsone gel plus clindamycin and benzoyl peroxide products—brown stains remained despite washing. Also, a pale-yellow residue was noticeable in all other dapsone gel–containing groups.

COMMENT

All benzoyl peroxide products used in this study, including the benzoyl peroxide creamy wash, 8%, and 2 different clindamycin, 1%, plus benzoyl peroxide gel, 5%, produced a discoloration reaction when mixed with either sulfacetamide or dapsone gel. Based on these results, both sulfacetamide and dapsone gel share a similar reaction with benzoyl peroxide, although the exact chemical reaction is unclear.

Because topical medications are frequently used in combination for the treatment of acne, these results are useful in understanding the possible reactions caused by the use of various topical acne medications. In these cases, it would be beneficial to use the medications at different times of the day and to encourage patients to completely wash off the benzoyl peroxide before applying other topical agents. Educating patients by warning them about the discoloration and inactivation reactions may help stress adherence to the designated treatment plan. Emphasizing the possibility of clothing stains would also deter patients from drifting from the prescribed regimen. Dapsone alone, at least on cloth, can impart a slight color. Unlike cloth, skin does not appear to be discolored by dapsone gel monotherapy or by dapsone in combination with non–benzoyl peroxide–containing prod-

![Figure 1. Chemical structures of dapsone, sulfacetamide sodium, and benzoyl peroxide. A, Dapsone, International Union for Pure and Applied Chemistry (IUPAC) name: 4,4'-sulfonyldianil. Molecular formula: C14H14N2O2S. B, Sulfacetamide sodium, IUPAC name: N-acetyl-4-aminobenzensulfonamide; molecular formula: C8H9N2NaO3S. C, Benzoyl peroxide, IUPAC name: dibenzoylperoxide; molecular formula: C14H10O4.](image-url)
Developing treatment plans for their patients. Physicians are developing treatment plans for their patients.

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Dapsone gel has recently been marketed in the United States for the treatment of acne, and sulfacetamide is already being prescribed. It is important for dermatologists and other physicians to understand the possible reactions when they are being prescribed. It is important for dermatologists and other physicians to understand the possible reactions when they are being prescribed.

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Figure 2. Photographs of sulfacetamide sodium and dapsone combined with different acne medications on a white cotton napkin at 0 minutes and at 2, 4, 6, and 12 hours after application and after the napkin is washed.

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Author Contributions: Dr Fleischer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Fleischer. Acquisition of data: Dubina and Fleischer. Analysis and interpretation of data: Dubina and Fleischer. Drafting of the manuscript: Dubina and Fleischer. Critical revision of the manuscript for important intellectual content: Fleischer. Administrative, technical, or material support: Fleischer. Study supervision: Fleischer.

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REFERENCES


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