# A New Standardized Method of Evaluating Cutaneous Irritation From Topical Medications

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*We used a new technique to evaluate and compare cutaneous irritation from various topical medications. Twenty participants with corticosteroid-responsive dermatoses were enrolled. Three target areas of unaffected skin were abraded. A negative control (petrolatum ointment), a positive control (an over-the-counter [OTC] anti-itch preparation containing benzyl alcohol), and a test product (fluticasone propionate lotion 0.05%) were each applied to separate target areas on the legs. Participants rated the irritation of each target area using a 10-point scale (1 [no symptoms] to 10 [intolerable burning/stinging requiring removal of the medication]). The mean irritation scores for petrolatum ointment, the OTC anti-itch preparation, and fluticasone propionate lotion 0.05% were 1.20, 6.15, and 2.05, respectively. The difference in irritation between the OTC anti-itch preparation and fluticasone propionate lotion 0.05% was highly significant (P<.0001). The difference in irritation between the OTC anti-itch preparation and petrolatum ointment also was highly significant (P<.0001). The difference in irritation between fluticasone propionate lotion 0.05% and petrolatum ointment also was statistically significant (P=.0104). Irritation scores were then standardized on a 10-point scale, with the irritation score of the negative control given a value of 1.00 and the irritation score of the positive control given a value of 10.00. The standardized irritation score of the test product, fluticasone propionate lotion 0.05%, was calculated to be 2.55. Our assay was able to detect and quantify even minimal cutaneous irritation secondary to application of topical medications.*

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Topical medications often are the first line of treatment for many dermatologic conditions. Unfortunately, many preparations contain ingredients that have the potential to cause irritation. Patients with a damaged skin barrier, inflammatory skin conditions (eg, psoriasis, eczema, rosacea), or sensitive skin are particularly susceptible to the irritation caused by topical medications.

In this study, we used a new technique to evaluate and compare cutaneous irritation from various topical medications. In addition, because patients vary in their assessments of irritation caused by topically applied medications, we created a method for standardizing irritation scores. A dimethicone-containing topical corticosteroid, fluticasone propionate lotion 0.05%, was used as a test product. It was compared with petrolatum ointment, which

served as a negative control. An over-the-counter (OTC) topical anti-itch preparation containing benzyl alcohol and indicated for the relief of pain and itching associated with inflammatory dermatoses was used as a positive control because of its irritant potential.

## Methods and Materials

Prior to study initiation, institutional review board approval was obtained and all participants provided written informed consent. Twenty participants with corticosteroid-responsive dermatoses were enrolled. Three 3-$cm^2$ areas of unaffected skin on the legs were abraded by a new disposable razor using 10 upward strokes; 2 target areas were chosen on one leg and 1 target area was chosen on the opposite leg. Following abrasion, a drape was placed in front of the participants to prevent them from viewing application of the study medication. Fluticasone propionate lotion 0.05% was applied to one target area, petrolatum ointment was applied to the second target area, and the OTC anti-itch preparation was applied to the third target area. Participants then rated the irritation of each target area on a scale of 1 (no symptoms) to 10 (intolerable burning/stinging requiring removal of the medication) at 1 minute postapplication. Statistical evaluations were performed, and standardized irritation scores for each product were calculated.

## Results

All 20 participants that were enrolled completed the study. Of note, 9 of 20 participants experienced no irritation following application of fluticasone propionate lotion 0.05%, despite abrasion of the skin. The mean irritation score for fluticasone propionate lotion 0.05% was 2.05; mean irritation scores for petrolatum ointment and the OTC anti-itch preparation were 1.20 and 6.15, respectively. Results are summarized in Figure 1.

Using standard parametric repeated-measures analysis of variance, the difference in irritation between the OTC anti-itch preparation and fluticasone propionate lotion 0.05% was demonstrated to be highly significant ($P<.0001$). The difference in irritation between the OTC anti-itch preparation and petrolatum ointment also was highly significant ($P<.0001$). Furthermore, fluticasone propionate lotion 0.05% was found to be slightly more irritating than petrolatum ointment ($P=.0104$).

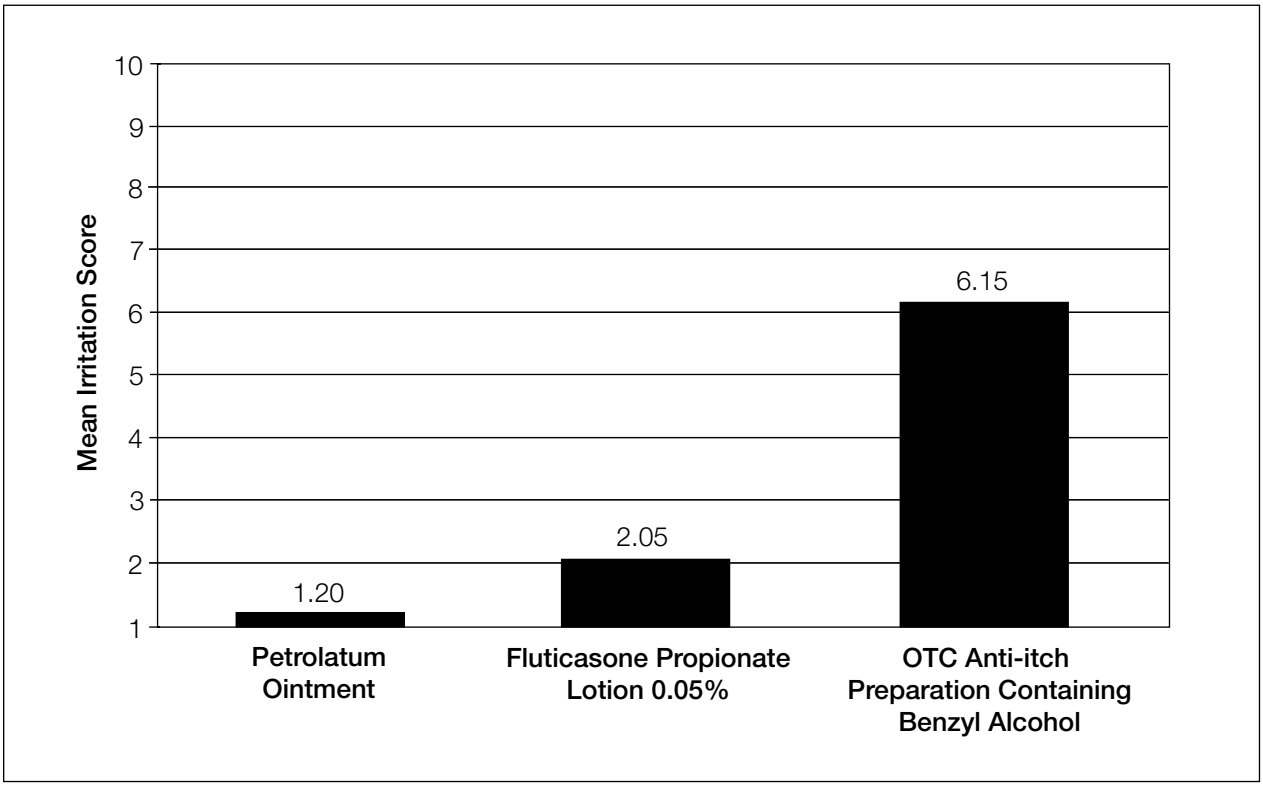


**Figure 1.** A comparison of the irritation caused by topical preparations. Irritation ratings were conducted 1 minute postapplication and rated on a scale of 1 (no symptoms) to 10 (intolerable burning/stinging requiring removal of the medication). OTC indicates over-the-counter.

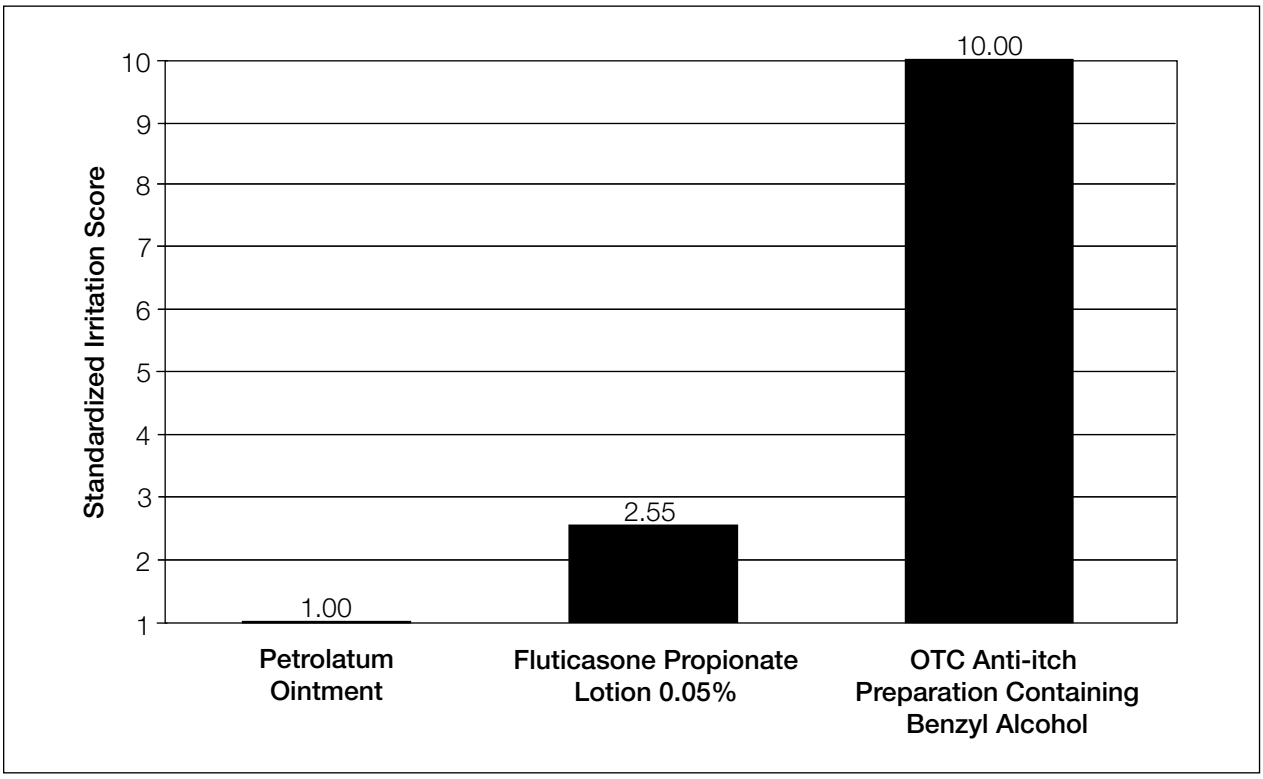


**Figure 2.** Standardized irritation scores on a scale of 1 to 10. OTC indicates over-the-counter.

Because patients vary in their assessments of irritation caused by topically applied medications, we sought to standardize the irritation scores on a 10-point scale, with the irritation score of the negative control (petrolatum ointment) given a value of 1.00 and the irritation score of the positive control (OTC anti-itch preparation) given a value of 10.00. The standardized irritation score of the test product (fluticasone propionate lotion 0.05%) was calculated as follows: $[(P-T)/(T-N)]=[(10-X)/(X-1)]$, where P indicates the mean irritation score of the positive control (6.15); N, the mean irritation score of the negative control (1.20); T, the mean irritation score of the test product (2.05); and X, the standardized irritation score of the test product. Using this formula, the standardized irritation score of the test product was determined to be 2.55 (Figure 2).

By testing a wide range of commonly used topical medications with our assay and compiling the standardized irritation scores, we hope to eventually create an irritation ranking system. This simple and straightforward scale ranging from 1 to 10 will provide physicians with an indispensable tool. As particular skin conditions are more susceptible to cutaneous irritation caused by topical medications, our ranking system may prove to be crucial in the selection of less irritating topical medications, thereby increasing patient compliance, comfort, and satisfaction.

## Comment

Although topical medications often are the first line of treatment for various dermatologic conditions, these patients may be especially sensitive to topical formulations. Our assay of fluticasone propionate lotion 0.05% was able to detect and quantify even minimal cutaneous irritation secondary to application of this topical medication. This new assay and method of standardizing irritation scores may be used in the future to determine the irritability of various topical preparations and produce a potential irritation ranking system. This system would not only enable clinicians to objectively choose less irritating topical medications for patients with damaged skin barriers but also would have the potential to increase patient adherence and compliance to treatment regimens.