

Strontium nitrate suppresses chemically-induced sensory irritation in humans

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Skin care products are complex formulations that may cause sensory irritation symptoms, characterized by stinging, burning, and itching. Substances capable of counteracting sensory irritation are of great practical interest. Strontium salts have been demonstrated to inhibit sensory irritation and inflammation when applied topically. In this double-blind study, we evaluated the efficacy of strontium nitrate in reducing chemically-induced skin sensory irritation in 8 subjects. In a random order, 20% strontium nitrate in 70% glycolic acid (pH=0.6) (mixture) was applied to the volar aspect of the forearm and a positive control (70% glycolic acid, pH=0.6) to the contralateral forearm. The irritation sensation was evaluated each min for the first 20 min after topical application using a scale from 0–4. The duration of the irritation sensation in min was also recorded. Strontium nitrate mixed with glycolic acid, in comparison with glycolic acid alone, markedly ($p<0.01$) shortened the duration of the irritation sensation from 24.4 ± 4.1 (mean $\pm$ SEM) min to 8.9 ± 3.7 (mean $\pm$ SEM) min, and significantly ($p<0.05$) reduced the mean magnitude of the irritation sensation at all time points (overall). The study demonstrated that strontium nitrate potently suppresses the sensation of chemically-induced irritation.

Key words: sensory irritation; alpha-hydroxy acids (AHAs); glycolic acid; strontium nitrate.
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Adverse effects of skin-care products include irritation (objective and/or subjective), contact allergy, photosensitivity, and contact urticaria (1). Chemically-induced “sensory irritation” (stinging, burning, and itching) is common. Although such symptoms are usually mild, they may cause the patient/consumer to discontinue using such products.

α -hydroxy acids (AHAs) significantly improve the appearance of photoaged skin and are widely used in the cosmetics industry (2–6). Many reports have indicated that local application of glycolic acid may induce varying degrees of irritation reactions, especially at higher concentrations (3, 6, 7). In a double-blind study, we evaluated the effects of strontium nitrate, that has been demonstrated to inhibit sensory irritation and inflammation when applied topically (8–11), in reducing 70% glycolic acid (pH=0.6)-induced sensory irritation in human skin.

Materials and Methods

Subjects

8 healthy Caucasians (4 men and 4 women) with an average age of 42 ± 7 (mean $\pm$ SD) years participated in this study after providing informed consent. The University of California San Francisco Human Research Committee approved the study.

Materials

20% strontium nitrate in 70% glycolic acid (pH=0.6) (mixture) and unbuffered 70% glycolic acid (pH=0.6) were provided by Cosmederm Technologies, Inc. (La Jolla, CA).

Methods

The middle of the volar forearm, approximately 10 cm from both the wrist and antecubital fossa, was

Table 1. Scale for irritation sensation such as stinging, burning, and itching

Scale	Irritation sensation	Definition
0	none	no stinging, burning, or itching
1	slight	intermittently perceptible stinging, burning, or itching, but not bothersome
2	mild	definite and continuous stinging, burning, or itching, bothersome
3	moderate	distinctly uncomfortable stinging, burning, or itching, constantly aware of irritation, interfering with concentration
4	severe	continuous stinging, burning, or itching, intensely uncomfortable, that would interfere with daily routine

selected as the test site. In a double-blind manner and in random order, 50 μ l of 20% strontium nitrate in 70% glycolic acid (mixture) was applied to the volar forearm and 50 μ l of 70% glycolic acid (positive control) to the contralateral forearm. All test materials were spread with a pipette tip over the marked 4 $\times$ 6 cm area. After topical application of the different substances, the irritation sensation was recorded and evaluated each min for the first 20 min using a scale from 0–4 (Table 1). The duration of the irritation sensation was also noted. The procedure was completed in one forearm before testing was started in the contralateral forearm.

Statistics

The Wilcoxon signed rank test was used to analyze the scores magnitude and duration of the irritation sensation. All analyses were performed using the StatView[®] software package (Abacus Concepts, Inc., Berkeley, CA).

Results

The irritation sensation for the strontium nitrate/glycolic acid mixture was always less than that for glycolic acid alone (overall and for all subjects) (Fig. 1). The difference was statistically significant ($p<0.05$) at each min for the 20 min measured, except at 1 min ($p=0.08$), 5 min ($p=0.09$), and 16 min ($p=0.12$). The difference between the mean scales for the 2 treatments (Fig. 1) steadily increased over time, peaking at a mean difference of 1.5 scale-points at 18 min ($p=0.0008$).

Strontium nitrate/glycolic acid mixture significantly ($p=0.003$) shortened the duration of the irritation sensation, in comparison with the 70% glycolic acid alone treated site, from 24.4 ± 4.1

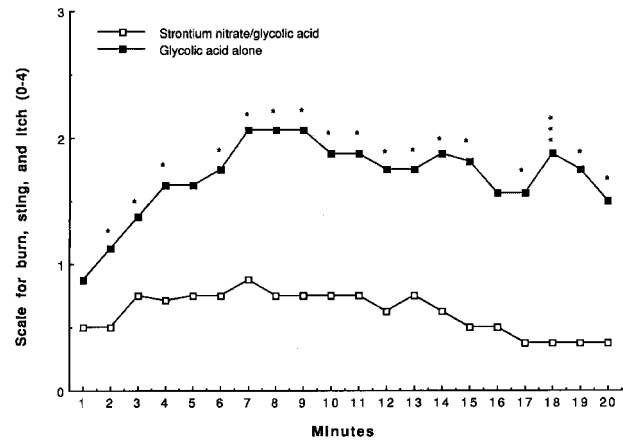


Fig. 1. Effects of strontium nitrate/glycolic acid mixture versus glycolic acid alone on chemically-induced irritation sensation. Values were expressed as the mean scales. * $p<0.05$; *** $p<0.001$.

(mean $\pm$ SEM) min to 8.9 ± 3.7 (mean $\pm$ SEM) min. The range for duration of the irritation sensation was 12 to 45 min for glycolic acid alone, whereas it was only 0 to 24 min for the strontium/glycolic acid mixture.

Discussion

AHAs have been widely used in cosmetic formulations and may cause stinging, burning, and itching (3, 6, 7). 70% glycolic acid solutions are commonly used as superficial chemical peeling agents with pH ranging from 0.08 to 2.75 (7). Becker et al. (7) reported the higher concentration acids (70%) and lower pH (below 2) created more irritation and tissue damage. Caution is therefore required when topically applying higher concentrations of glycolic acid. To prevent or reduce irritation and adverse effects, adding irritation inhibitors or partially neutralized glycolic acid solutions may prevent or/and reduce irritation and other adverse effects. Modifying the formulation or raising the pH may, however, reduce efficacy. Strontium salts have been reported to inhibit and reduce sensory irritation, without altering the pH of the preparation, when applied topically (8–11). In this study, we observed that the 20% strontium nitrate in 70% glycolic acid significantly reduced sensory irritation and duration when compared with the 70% glycolic acid (pH=0.6) treated site (control).

Since sensory irritation is a subjective symptom, there is a high degree of variation between individuals. To quantify this subjective data better, we utilized a 0–4 grade scale, and measured every min for the first 20 min post-application of test materials. We believe this scale is

better able to quantify small changes in subjective responses.

The mechanism of the inhibitory effect of strontium remains unclear. We hypothesize that strontium directly affects the type C nerve depolarization known to transmit itch, burn and sting information, independent of the chemical nature of the applied stimulus (8, 12–13).

Our data show that the addition of strontium nitrate to 70% glycolic acid (pH=0.6) significantly reduces the sensory irritation, and suggests that strontium nitrate may be useful as an inhibitor in such formulations. Clinical studies have confirmed that strontium nitrate does not interfere with the efficacy of glycolic acid, as assessed by clinical observation and skin biopsy (9–11).

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