

# Strontium Nitrate Decreased Histamine-Induced Itch Magnitude and Duration in Man

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## Key Words

Antipruritic effects · Histamine · Strontium nitrate · Visual analogue scale

## Abstract

**Background:** Previous studies have demonstrated that strontium salts have a potent and broad ability to suppress sensory irritation. **Objective:** To ascertain the possible antipruritic effects of topical strontium salts, we conducted a double-blind randomized study to evaluate the effect of 20% strontium nitrate on itch magnitude (intensity) and duration. **Methods:** In 8 human subjects, strontium nitrate was applied to the volar forearm and vehicle control to the contralateral volar forearm for 30 min; both substances were reapplied for an additional 5 min. Itch was then experimentally induced by intradermal injection of histamine. Itch magnitude was rated each minute for the first 20 min using a visual analogue scale (VAS). Itch duration in minutes was also recorded. **Results:** Strontium nitrate, in comparison to its vehicle control, significantly shortened itch duration from  $28.1 \pm 5.4$  min (mean  $\pm$  SEM) to  $18.5 \pm 4.2$  min ( $p < 0.01$ ) and reduced itch magnitude at time points 12–20 min and overall ( $p < 0.05$ ). **Conclusion:** Strontium nitrate may act as a topical antipruritic agent in reducing histamine-mediated itch.

## Introduction

The itch sensation can be elicited by chemical, mechanical, thermal and electrical stimuli [1–3]. Mediators of itch presumably act directly on nerve fibers or lead to a nerve stimulation cascade whose final common pathway is interpreted in the central nervous system as itching [3]. Numerous chemicals evoke itch such as histamine or substance P [2]. Histamine, the prototypical chemical mediator of itch, is released during mast cell degranulation and mediates its effects in the skin via H<sub>1</sub> receptors [3].

Recently, strontium salts have been demonstrated to have a potent and broad ability to suppress sensory irritation caused by many chemically and biologically unrelated irritants [4, 5]. We attempt to assess if strontium may act as an antipruritic when applied topically. This study evaluates the effect of strontium nitrate on histamine-induced itch duration and magnitude.

## Materials and Methods

### Subjects

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

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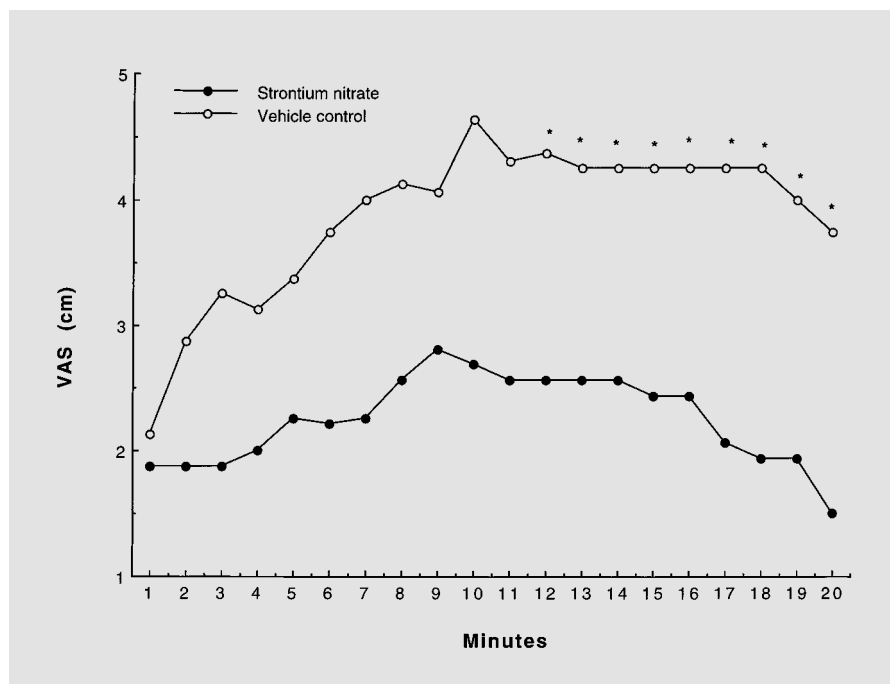
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1018–8665/00/2003–0244\$17.50/0

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**Fig. 1.** Effect of strontium nitrate versus vehicle control on histamine-induced itch magnitude. Values were expressed as the means (cm) of the VAS. \*  $p < 0.05$ .

#### Materials

Twenty percent strontium nitrate was prepared in sterile water (Cosmederm Technologies Inc., La Jolla, Calif., USA). The vehicle control was sterile water. Histamine dihydrochloride (Sigma, St. Louis, Mo., USA) was prepared as 100  $\mu\text{g}$  histamine in 1 ml 0.9% sodium chloride (Baxter, Deerfield, Ill., USA).

#### Treatment

The forearms, approximately 10 cm from wrist and antecubital fossa, were the test sites. In a double-blind and random manner, 50  $\mu\text{l}$  of 20% strontium nitrate was applied to one forearm and 50  $\mu\text{l}$  of vehicle control (sterile water) to the contralateral forearm for 30 min. Both were reapplied for an additional 5 min. Test materials were spread with a pipette tip over the marked 4  $\times$  6 cm area. At 35 min, 1 ml of histamine solution (100  $\mu\text{g}$  histamine dissolved in 1 ml normal saline) was injected intradermally into the test site using a 1-ml single-use insulin syringe (Becton-Dickinson, Franklin Lakes, N.J., USA). Subjects were asked to grade the itch magnitude (intensity) at 1-min intervals for the first 20 min after histamine injection by using a visual analogue scale (VAS) ranging from 0 to 10 cm [6]. On this scale, 0 was defined as 'no itch sensation' and 10 as 'maximum itch sensation'. Itch duration in minutes was also recorded.

#### Statistics

The Wilcoxon signed rank test was used to analyze the itch magnitude and itch duration data. All analyses were performed using the StatView<sup>®</sup> software package (Abacus Concepts Inc., Berkeley, Calif., USA).

## Results

#### Itch Magnitude

In comparison with its vehicle-control-treated site, strontium nitrate significantly ( $p < 0.05$ ) reduced itch magnitude at 9 time points (minutes 12–20 and overall). The mean difference in itch magnitude between the two sites steadily increased, reaching a maximum at the last time point, 20 min (fig. 1). The VAS scores at 20 min were  $2.2 \pm 0.2$  cm (mean  $\pm$  SEM) for the strontium-treated site and  $3.8 \pm 0.3$  cm (mean  $\pm$  SEM) for the vehicle-control-treated site, i.e. a 42% reduction in itch.

#### Itch Duration

Strontium nitrate significantly decreased ( $p < 0.01$ ) itch duration in comparison with its vehicle control from  $28.1 \pm 5.4$  min (mean  $\pm$  SEM) to  $18.5 \pm 4.2$  min.

## Discussion

We utilized the histamine-induced itch model because acute itching is most commonly evoked by chemical stimuli (e.g. histamine) [2]. This model, adopted in previous studies, has been described in detail [6–10]. From these data, we conclude that topical strontium nitrate signifi-

cantly reduces the magnitude and duration of histamine-induced itch.

Since itch is a subjective symptom, its magnitude (intensity) may only be estimated from subjective reports from patients or volunteers and, therefore, there is a high degree of variation between individuals. To better quantify these subjective data, we employed a VAS scale. VAS scales are widely believed to better identify and quantify small changes in subjective responses than other scales [6].

Topically applied strontium salts are effective in suppressing stinging, burning and itching caused by many acidic, neutral and basic chemical irritants found in cosmetics, personal care products and pharmaceuticals [4, 5]. The mechanism for the antipruritic effect of strontium is unclear. One possible explanation is that strontium may

be directly affecting the C fibers that transmit pain and itch signals. Thirty-five minutes after strontium application, we observed a significant decrease in the itch sensation, implying that a sufficient quantity of strontium penetrates the skin to achieve an effective concentration.

In conclusion, strontium nitrate is a potent topical antipruritic agent that reduces the subjective duration and magnitude of itching. Further study to explore its exact mechanisms of action is warranted; its application in clinical dermatology deserves investigation.

### Acknowledgement

Hilda Maibach provided statistical advice.

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