

# Safety and Effectiveness of an L-Lysine, Zinc, and Herbal-Based Product on the Treatment of Facial and Circumoral Herpes

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## Abstract

**CONTEXT:** L-lysine, an essential amino acid, inhibits normal replication of *Herpes simplex virus* (HSV), shortening the normal course and duration of the disease. This study was conducted to determine the effectiveness of a combination of L-lysine with botanicals and other nutrients in relieving the symptoms of facial and circumoral herpes. **METHODS:** This small pilot study was conducted using an outcome (open-label) model. Thirty male and female participants (15 in each group) meeting the inclusion/exclusion criteria were admitted to the study. The 10 outcome measures used to monitor the sores were tingling, itching, burning, tenderness, prickling, soreness, bump/swelling, small blister(s), oozing blister(s), and crusting, as well as before-and-after photographs of the lesion, and a daily diary. **RESULTS:** At the end of treatment the ointment produced full resolution in 40 percent of the participants by the third day and in 87 percent by the end of the sixth day. A cold sore episode may last up to 21 days without treatment. **CONCLUSIONS:** Overall data indicated significant improvement in participants by the sixth day of treatment for all but two participants. There were no adverse effects reported during this study. (*Altern Med Rev* 2005;10(2):123-127)

## Introduction

*Herpes simplex* labialis, more commonly known as a cold sore, is caused by *Herpes simplex* virus type-1 (HSV-1). It is a common recurrent disease affecting 40 percent of the population worldwide.<sup>1</sup> After primary infection the virus resides in the associated dorsal root ganglion and establishes a long latency period. This is the period during which the infectious virus cannot be detected with standard virus isolation procedures. External stimuli such as stress and immunosuppression usually initiate reactivation of the virus from dormancy.<sup>2</sup> For many, a herpes virus recurrence represents a nuisance; however, for immunocompromised individuals (with HIV, for

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example) this infection is associated with increased morbidity and mortality.<sup>3</sup> Individuals with severe immunosuppression were excluded from participation in this study.

The virus travels along the endoneural sheath to the skin surface and causes maculopapular vesicular eruptions around the lips. The eruption is usually associated with tingling, burning, and discomfort, as well as more generalized signs and symptoms, such as nausea or fever. In general, the episode lasts 7-10 days and is completely healed without intervention within 21 days.<sup>4</sup> These factors necessitate treatment of the lesion as they can cause interference with eating and speaking, and also have a psychosocial impact.

The essential amino acid, L-lysine, has been shown to inhibit normal replication of HSV, shortening the course and duration of the disease. When a topical application of crystalline L-lysine on cutaneous HSV inoculations and subsequent dorsal root ganglia infection was studied in male Hartly guinea pigs, L-lysine-treated skin remained clinically normal; whereas, untreated controls manifested clinical symptoms up to three days post-inoculation.<sup>5</sup> In another study performed by Griffith et al, L-lysine antagonized the viral growth-promoting action of arginine, thereby decreasing viral load *in vitro*.<sup>6</sup>

These results are in accord with a multi-centered study in which 312-1,200 mg daily oral L-lysine in single or multiple doses to 45 patients accelerated recovery from *Herpes simplex* infection and suppressed clinical manifestations of the disease and its recurrence.<sup>7</sup> Langeland et al also reported that *in vitro* polylysine (a homopolymer of L-lysine) blocked the binding of HSV-1 by interfering with cellular receptor function.<sup>8</sup> Based on these data, it was postulated a lysine-based topical cream could have a positive effect on decreasing the length of time needed for circumoral herpes resolution, the signs and symptoms associated with it, and its recurrence rate. However, there are few studies on the combination of L-lysine with botanicals and other nutrients.

This study examines the effectiveness and safety of SuperLysine Plus+<sup>®</sup>, a combination of L-lysine and 16 other ingredients, in relieving the symptoms of facial and circumoral herpes.

## Materials and Methods

### Product Description

SuperLysine Plus+ cream, manufactured by Quantum Health, Inc., consists of L-lysine combined with zinc oxide, lithium carbonate 3X, propolis extract, calendula flower extract, echinacea flower extract, goldenseal extract, vitamins A, D, and E in a natural olive oil base, yellow beeswax, cajuput oil, tea tree oil, gum benzoin tincture, and honey. L-lysine, zinc oxide,<sup>4</sup> lithium carbonate,<sup>9,10</sup> propolis extract,<sup>11</sup> echinacea extract,<sup>12,13</sup> and other ingredients in SuperLysine Plus+ cream have been shown to be of clinical value for treating facial and circumoral herpes infection.<sup>14-17</sup>

### Subjects

Overall, 120 participants from the greater Los Angeles area who reported a history of cold sores were pre-registered for the study. The first 30 pre-registered persons who met the protocol requirements and presented on baseline measurement with signs and symptoms of a cold sore consistent with HSV infection of  $\leq 24$ -hours duration participated and completed the study. On-site clinicians evaluated participants to confirm the presence of facial or circumoral herpes and that the participants met all study requirements. The sample selection was based on the following inclusion criteria: (1) participant had signs and symptoms of HSV infection and presented within 24 hours to the Southern California University of Health Sciences Research Division; (2) participants were ages 18-65 years; (3) confirmation of facial or circumoral herpes lesion was completed by a clinician on site; (4) subjects expressed willingness to satisfactorily complete a patient diary for the length of the study (maximum of 21 days); (5) subjects were willing to have the presenting lesion photographed twice; and (6) subjects signed a written informed consent.

Participants were excluded from the study for any one of the following reasons: (1) history of past or present immunosuppressive condition, either due to a disease or immunosuppressive medication; (2) history of adverse effects or allergies to any L-lysine-based/zinc oxide product and/or cream base containing any of the other ingredients; (3) evidence

of any other dermatological diagnosis; (4) signs of disseminated HSV illness; (5) history of use of oral or topical antiviral agents within 10 days of entry into the study and/or at first study visit; or (6) pregnancy or lactation.

**Table 1. Number of Patients Reporting Cure for each Study Day (Baseline through Day 11)**

Day	0	1	2	3	4	5	6	7	8	9	10	11
Number	0	4	7	12	17	22	26	26	26	27	28	30

### Outcome Measures

The 10 symptoms – tingling, itching, burning, tenderness, prickling, soreness, bump/swelling, small blister(s), oozing blister(s), and crusting – as well as photographs (baseline and end of study) and daily diary were used as outcome measures in this study. The study also utilized the factor of “cure” as an outcome measure to determine the healing of a cold sore. This variable refers to the complete disappearance of the lesion, not merely crusting. When there is a cure in less than four days, individuals may not experience crusting. This healing pattern is often reported in the literature as an aborted event.<sup>18</sup> In this study, those who did not experience an aborted lesion were considered cured when full crusting occurred. The daily diary monitored the cold sore symptoms on a 10-point scale (0-10), with zero being no symptom and 10 being worst symptom (example: 0=no tingling ... 10=worst tingling).

### Data Collection

The participants had a digital photo taken of the lesion and received the initial product application on site at the time of the first visit. They were instructed to apply the lysine-based product, using a clean fingertip, over the cold sore at two-hour intervals during waking hours each day until the sore crusted or disappeared. Study recruits rated signs and symptoms in the symptom diary before reapplying the product at two-hour intervals. If a cure was declared, the patient was asked to report to the Research Division within 24 hours, and submit the diary and the balance of unused product as a compliance validation. At that time a second photo of the lesion site was taken for validation of effectiveness.

### Results

In this study both genders were equally represented. However, the age range for males and females was divergent; the female group had a mean age of 40 compared to a mean age of 28 for males.

Table 1 describes how many days it took for the cold sores to reach a “cure,” emphasizing the number of participants who experienced a “cure” by the end of days 1, 3, and 6 of treatment. These days were chosen arbitrarily as fixed markers. Baseline was set as day 0. On the first day, four participants who reported with signs and symptoms of cold sore of less than 24 hours recorded cure. By the third day of treatment, lesions had cured in 12 participants (40%). By day 6, 26 participants (87% of sample) reported cure, and by day 11, all participants reported cure. These percentages are cumulative.

To construct the data for cold sore symptoms, any study participant who was “cured” received a value of zero for all cold sore symptoms for the remainder of the study days. As such, the data analyses reported in Table 2 are for all 30 participants. Table 2 presents data on symptoms of cold sores. Symptoms rated on a 10-point scale are the first seven items in the table. The next two items indicate the number of small and oozing blisters. The last item included in Table 2 is a constructed variable, which is the mean of symptoms 1, 3, and 4 (severity of tingling, burning, and tenderness). Results indicate a significant improvement ( $p < 0.001$ ) between baseline (0 day) and day 3 for this constructed variable. Except for the number of oozing blisters, all other symptoms showed significant improvement ( $p < 0.001$ ) by the end of the third day. Data between baseline and day 6 was also compared, and all symptoms showed improvement by the sixth day ( $p < 0.001$ ).

**Table 2. Cold Sore Diary – Comparison Rates of Symptoms between Baseline and Days 3 and 6**

Symptom	Baseline (Day 0)	Day 3 <sup>^</sup>	Day 6 <sup>^^</sup>
Tingling (T)	3.90	1.00*	0*
Itching	2.63	0.87*	0*
Burning (B)	2.97	0.77*	0*
Tenderness (T)	4.07	1.93*	0.43*
Prickling	2.57	0.60*	0*
Soreness	3.67	1.70*	0.47*
Bumps/Swelling	3.93	1.63*	0.37*
# of small blisters	2.53	1.20*	0.17*
# of oozing blisters	0.93	0.70 ns	0*
Combined TBT symptoms	3.64	1.24*	0.15*
N		n=30	n=30

<sup>^</sup> The day 3 column compares baseline to day 3.

<sup>^^</sup> The day 6 column compares baseline to day 6.

\* p-values < 0.001 – based on Paired-Samples T Test.

ns = not significant

## Conclusion

This product produced a “cure” as defined above in 40 percent of the study participants by the end of the third day, and in 87 percent of the participants by the end of the sixth day. All lesions were cured by day 11. Differences in self-reporting of the two factors concerning blister counts are likely due to the descriptors used for the symptoms: small versus oozing. No adverse events were reported during the trial period. This study only evaluated the safety and effectiveness of a single product: SuperLysine Plus+. Due to the preliminary nature of this study, a small sample size was used and therefore no definitive statements can be made. A larger, heterogeneous, double-blind, randomized, controlled clinical trial is necessary in order to definitively determine the efficacy of this product.

## Disclosure

This study was funded by Quantum, Inc., Eugene, OR. SuperLysine Plus+ is a licensed product of Quantum, Inc. No person in the Southern California University of Health Sciences Research Division has a financial interest in the product or the sponsoring company.

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