



Registered charity 291657

# Herpes Viruses Association

41 North Road London N7 9DP  
Office Tel: 020 7607 9661 Helpline: 0845 123 2305  
e-mail: [marian@herpes.org.uk](mailto:marian@herpes.org.uk)

## Double-blind Comparison of Liquorice-root Based Balm (Liquorice Balm) and Placebo Preparation - A Consumer Study

Authors: Dr D. Grant MBChB, General Practitioner  
Marian Nicholson, Director of the Herpes Viruses Association

Date 1<sup>st</sup> June 2008

### **Abstract**

Laboratory work has demonstrated in vitro activity of liquorice root extract against viruses including herpes simplex virus type 1.<sup>i</sup> This virus causes cold sores on the face and, through oral sex, is increasingly the cause of genital herpes infection.<sup>ii</sup> This trial showed the positive effect of liquorice balm (see footnote \*) in preventing cold sores and genital sores.

Key words: herpes simplex, treatment, liquorice root, cold sores, genital sores.

### **Introduction**

A study was performed with the Herpes Viruses Association to see whether there was any evidence that a topical liquorice based cream would be as effective against herpes simplex in subjects as it had proved to be in vitro, in a laboratory. These are referred to as "cold sores" throughout for brevity.

### **Conflict of Interest**

Dr Grant asserts there are no conflicts of interest. The randomisation details were held by one individual who broke the randomisation code after the analysis was performed. Full details of the randomisation process were made available to him.

### **Study Design**

The study was conducted as a double-blind, placebo-controlled trial. The placebo was designed to be as pleasant as possible so that users would not be able to distinguish it from the study treatment.

### **Recruitment**

Recruitment was through an advertisement placed on the Herpes Viruses Association website. It asked for people who would be interested in taking part in a placebo-controlled trial into a natural cold sore treatment. Respondents were vetted for frequency of outbreaks (>6 p.a.) and their willingness to be on a placebo-controlled trial in which they might not receive an active treatment.

The sample was randomised to either placebo or test substance (liquorice balm)

Funding from  
the Department  
of Health

Patrons: Professor Michael W Adler CBE MD FRCP FFCM  
Dr B A Evans FRCP, Dr Colm O'Mahony MD FRCP BSc DIPVen  
Dr Elizabeth Claydon MRCP MB ChB, Dr David Barlow MA BM FRCP  
Dr Miriam Stoppard MD FRCP, Dr David Bull MBBS BSc, Dr Phil Hammond MB BChir MRCGP

Numbers: 37 subjects were recruited, 26 women and 11 men. The lesions affected a variety of sites including mouth, genitals and anus. 28 individuals developed an outbreak of herpes simplex sores during the study period – which will be referred to as “cold sores” throughout. 3 people (2 women, 1 man) did not have any outbreaks during the study period but were able to comment subjectively on the preparation’s characteristics. 6 people (4 women, 2 men) dropped out of the trial: one because the product did not smell of liquorice (“and I know the real thing smells strongly”), one because “it made the symptoms worse”; one because there was no beneficial effect (“it’s like Vaseline”). When the trial was un-blinded, it was found that all the people who did not have outbreaks and all the drop-outs had been using the placebo cream.

The volunteers were asked what they had been using and what they thought of its effect. Their opinions are averaged out: 25 had used Zovirax/aciclovir cream (average score “helped, but only a bit”); 11 had used lysine supplements (average score “helped, but only a bit”); 7 used aciclovir/Zovirax or Valtrex tablets (“helped quite a lot”); 7 used aromatherapy oils of various kinds (“helped, but only a bit”); 4 had used Lomabrit lemon balm cream (“helped quite a lot”); 3 used tea-tree oil (“helped, but only a bit”); 2 used EMLA anaesthetic ointment (“definitely helped”). Each of the following had been tried by one person and scored “helped” : Compeed patch, Anbesol anaesthetic cream, zinc, Fenestil antiviral cream, Choraphor lotion.

## **Analysis**

The figures were analysed using Decision Analyst TM statistical package.

### **1. Testing the subjective measurement – Is the substance real or the placebo?**

The respondents were asked whether the test product they were using was the real substance or the placebo. This was designed to check the suitability of the placebo. The placebo was designed to be a highly usable balm which would be pleasant to use and have a moisturising effect. It was designed to be similar to the actual liquorice balm except for the absence of an active ingredient.

The results were analysed by a paired comparison test (which indicates whether a difference between two responses occurs by chance).

The difference between two groups had a 63% probability that the percentages were different, rather than arising by chance. (Bear in mind 50% is flipping a coin)

The result of this test suggests that subjects could not discriminate between the test substance and the placebo and that the placebo was well chosen.

Respondents were also asked if their test product was pleasant to use. The liquorice balm testers responded with 93.3% and the placebo users responded with 77.8%.

### **2. Testing the subjective measurement – What is the value of the preparation?**

Respondents were asked to rate their test product from 0 to 10. For the placebo the mean value was 4, with a variance of 14. Variance is an indicator of how opinion varies within a group, a large value indicating significant disagreement and a small value indicating agreement. This suggests that people’s opinions differed widely over the value of the placebo. Testing the liquorice balm, the mean was 6.4 and the variance much less at 4.5 indicating a general agreement. The test for the difference between two means gave a 98.3% probability that there was a real difference between the populations. This is a statistically significant result.

Whilst the liquorice balm scored more highly than the placebo in all categories, the 17 people with facial cold sores were more satisfied with both liquorice balm (average score of 73%) and placebo (average of 38%), than the 17 people with genital sores (average scores of 60% for liquorice balm and 45% for placebo).

### **3. Testing the subjective measurement - Were your sores less severe?**

Respondents were asked whether their sores were less severe when using their test product. Of those using the liquorice balm, 73.3% felt their sores were less severe. For those using the placebo, 54.5% of respondents felt that their sores were less severe.

There was a 98% probability that the difference between two groups was due to the effects of the liquorice balm, rather than arising by chance. This is statistically significant and suggests that subjectively the subjects did feel there was a real difference between the two substances.

### **4. Testing the more objective measurement – What was the duration of the outbreak?**

Respondents were asked for the average duration of their cold sores before the trial. They were then asked to record the length of outbreaks during the trial. 83% of those using the liquorice balm recorded lower than average times for their outbreaks, i.e. shorter outbreaks than they had experienced using other treatments before the trial. For those using the placebo, 60% recorded a reduction in average times during the trial.

An actual comparison of the mean reduction in duration for those using the liquorice balm was 45% with a standard deviation of 25%. The mean reduction for the placebo was 15.7% with a standard deviation of 80%. There was far smaller variance between the liquorice balm testers regarding the shortening of duration.

One subject had an increase in normal duration while using the placebo which skewed the placebo results significantly. Testing by the same method as used in section 3. above (the difference between two means) gives a 75% probability that the difference is real (i.e. not statistically significant). Disregarding this one figure gave a 0% probability that the results were different.

### **Discussion**

This was a well designed study which was carried out without any obvious bias. There was significant agreement amongst users that the preparation was subjectively of value. Whilst the mean figures for reduction in duration were different between the two groups (with a 45% reduction in duration amongst those using the liquorice balm on average and a 22% average reduction using the placebo, the small sample size and the high standard deviation (with a range in the liquorice balm group of 0-71% reduction and in the placebo group an 88% reduction to a 180% lengthening) makes the figures almost impossible to interpret statistically.

However some figures do come out of the study which are of interest. The liquorice balm performed very strongly but so too did the placebo which was also of great benefit to respondents. The study was difficult to interpret partly because the placebo performed so strongly. This repeats previous findings that the use of a good moisturising balm is in itself an excellent treatment for cold sores.<sup>iii</sup>(3) It is certainly known that chapped or dry lips are more prone to cold sores.<sup>iv</sup> (Do you have a reference for this statement.)

The figures for average duration should also be viewed in the context that the all the respondents reported using other treatments to control their outbreaks prior to the trial. The comparison is not between outbreaks with or without treatment but between this new treatment and their former treatments. This actually makes the results more impressive for both the lip balm and the placebo. 73.3% of those testing the liquorice lip balm felt that their cold sores were less severe and objectively 83% actually experienced less severe outbreaks while using it.

It should also be noted that while the balm was not significantly statistically better than the placebo on some of the objective markers, it did achieve far less variance between its testers on the topic of its effectiveness in both subjective and objective measurements.

A future trial into a liquorice balm would be of interest to investigate any reduction in the number of outbreaks if used all the time, compared with placebo. In the laboratory liquorice is thought to be effective against non-replicating virus and encourages the death of those cells infected by herpes virus. On this basis one might expect fewer recurrences in those treated with balm than with placebo. It is likely that a larger study would be needed to demonstrate any statistical significance.

### Volunteers' comments

Comments from people using the liquorice balm on the face included:

"Worked brilliantly, but I gave up smoking at the same time" "Beneficial"

"Gave the details to a woman at work as she suffers badly. To find something that works this much is brilliant." "Not very good" "Bit greasy, though it feels nice" "It goes a long way, more than 1/2 tub left" "Greasy, eased the soreness"

Using placebo facially: "Bit better than regular salve, using it as lip cream"

Comments from people using the liquorice balm on the genitals/anus included: "It's very comfortable to use" "Really good – I'm going to buy it" "I would buy it and use it - if nothing else because outbreak is uncomfortable and this is so soothing."

Using placebo genitally/anally: "Using it daily definitely stopped outbreaks" "Very good; very effective" "Emollient, soothing" "Greasy, but it made a difference"

- i Licking latency with licorice. J. of Clinical Investigation. March 2005; **115**(3):591
- ii Scoular A, Norrie J, Gillespie G, Mir N, Carman WF. Longitudinal study of genital infection by HSV type 1 in Western Scotland over 15 years. *BMJ* 2002 June 8; **324**:1366-1367
- iii Update on drugs for herpes zoster and genital herpes. *Drug and Therapeutics Bulletin* 1998; **36**(10):77-79
- iv The prevalence of chapped lips during an army hot weather exercise. *Mil Med.* 1997 Dec; **162**(12):817-9.

**\* Liquorice balm used for this trial was provided by the Skin Shop and can be purchased at [www.skinshop.co.uk](http://www.skinshop.co.uk) for £7.99**

