

Effects of a Herbal/Homeopathic Topical Salve on Cutaneous Oxygenation in Type 2 Diabetes

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Abstract

Purpose: To assess the effects of Puremedy® Original Healing Salve (OHS), including 1X homeopathic dilutions of Calendula, Echinacea, and Sambucus extracts, plus extracts from pine and Balsam fir, on lower extremity cutaneous oxygen delivery measured as changes in transcutaneous oxygen pressure (TcPO2). **Methods:** Randomized, triple-masked, crossover trial to measure effects of Original Healing Salve on the TcPO2 in the skin of the lower extremity in people with type 2 diabetes without peripheral artery disease. Participants were assigned in random order to receive either the Original Healing Salve (test), or the salve base alone (control). After a 20 minute warm up cycle, the salve was applied and oximeter (Radiometer America, Inc.) readings were recorded from four sensors (two lower leg, and two foot) at 5 minute intervals for 30 minutes. The primary outcome was the difference in TcPO2 in the lower leg sensors between the test and control salves at 30 minutes after application by ANOVA. The secondary outcome was change in TcPO2 in the leg sensors from the application of the test salve by paired t-test. Exploratory analyses evaluated changes in TcPO2 at all time points and assessed for trends over time. **Results:** Sixteen participants with type 2 diabetes were randomized, and completed the trial. The mean difference in TcPO2 at 30 minutes in the leg sensors combined = 0.39 +/- 8.54, p=0.86. Within the test group, the mean change in TcPO2 at 30 minutes in the leg sensors = 3.70 +/- 6.62, p=0.04. There were no significant differences between the test and control salves at any time point. Significant linear and cubic trends were measured in both treatment groups, suggesting increases in TcPO2 over time. **Conclusions:** The Original Healing Salve increased TcPO2 after 30 minutes in people with type 2 diabetes, however the contributions of the herbal and homeopathic ingredients remain unclear.

Introduction

Poor wound healing, whether resulting from surgery or traumatic injury, leads to increased risk for infection and therefore increased risk for morbidity and mortality. In people with diabetes, poor wound healing can lead to systemic infection, ulceration, gangrene, and amputation.

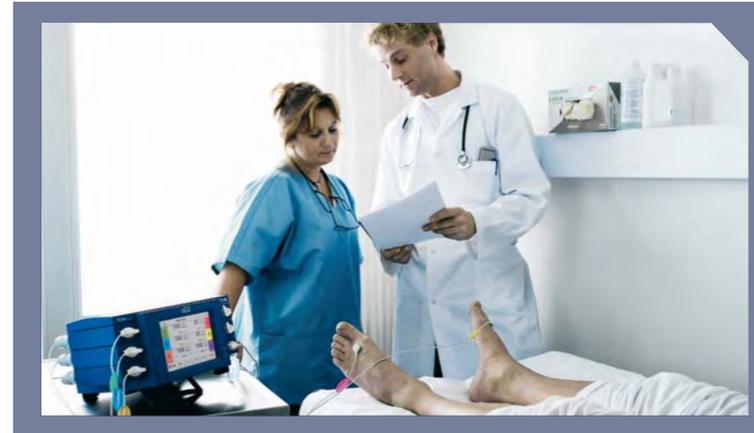
Wound healing is predicted by tissue oxygenation. Cutaneous oxygenation is assessed by the partial pressure of oxygen (TcPO2), which can be accurately measured. TcPO2 predicts wound healing time and subsequent risk for amputation.

Very little clinical evidence exists on the use of botanical medicines and extracts for wound healing. The experimental salve under evaluation in this study, Puremedy® Original Healing Salve (OHS), contains homeopathic amounts of *Calendula* (1X), *Echinacea* (1X), *Sambucus* (1X) and botanical extracts from pine and Balsam fir. Specific to these ingredients, marigold (*Calendula officinalis*) has one clinical trial supporting its therapeutic properties. Specifically, the application of a *Calendula*-extract containing ointment reduced the surface area of venous ulcers on average and resulted in complete epithelialization in some participants, which did not occur from placebo treatment. No clinical trial evidence is available for either *Echinacea* or *Sambucus* applied homeopathically or botanically, despite traditional use for skin health and wound care.

Figure 1: Balsam fir



Figure 2: Use of TCM400 Oximeter



Objectives

Specific Aim: To assess the effects of Puremedy® Original Healing Salve on lower extremity cutaneous oxygen delivery, measured as mean changes in transcutaneous oxygen pressure (TcPO2), in people with Type 2 diabetes.

Hypothesis 1: Puremedy® Original Health Salve will acutely increase transcutaneous oxygen pressure (TcPO2), when compared to salve base alone, in adults with type 2 diabetes.

Methods

We conducted a randomized, controlled, crossover, triple-masked clinical trial to measure the effects of Original Healing Salve (OHS) on the TcPO2 in the skin of the lower extremity in sixteen (n=16) generally healthy adults with type 2 diabetes without peripheral artery disease. Participants were assigned in random order to receive either the OHS (test), or the salve base alone (control) on different days, and then crossed-over to the other condition at least one week later. After a 20 minute warm up cycle, ½ oz. of salve was applied according to Figure 3 (below) and oximeter (TCM400, Radiometer America, Inc.) readings were recorded from four sensors (two lower leg, and two foot) at 5 minute intervals for 30 minutes.

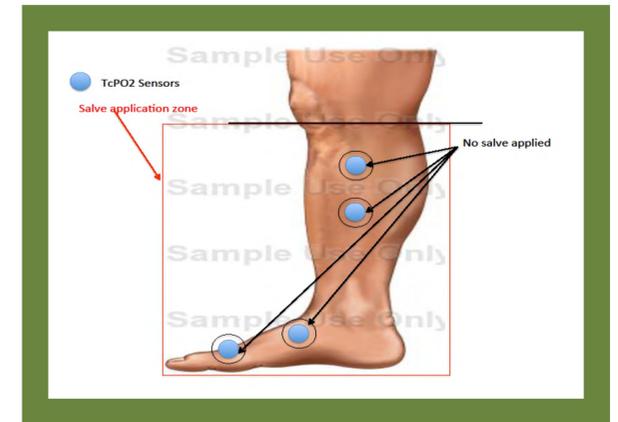
The primary outcome was the difference in TcPO2 in the lower leg sensors comparing test and control salves at 30 minutes after application. The secondary outcome was change in TcPO2 in the leg sensors at 30 minutes from the application of the test salve. Exploratory analyses evaluated changes in TcPO2 at all time points and assessed for trends over time. Simple differences between conditions or time points were assessed using paired t-tests; for temporal effects we used repeated measures ANOVA with linear trend analysis.

Our sample size (n=16) allowed for 80-90% power to detect a change in TcPO2 of 10% as statistically significant using a threshold of alpha=0.05. This sample size calculation is estimated based on published mean TcPO2 values for healthy adults, i.e., 41.3 +/- 3.5 mmHg for the lower leg.

Table 1: Study Procedures

Study Visit	Telephone Screening	Screening Visit	Visit 1	Visit 2
Consent for study participation		X		
Inclusion/ Exclusion criteria	X	X		
Physical exam of lower legs to check for edema, rashes, ulcerations		X	X	X
Allergy screen – test application of active salve		X		
Standardized Multi-system AE Questionnaire		X		
Standardized Skin Reaction Questionnaire		X	X	X
Walking Impairment Questionnaire	X			
Vitals/Anthropometrics		X		
Active or Placebo Salve Applied			X	X
TcPO2: pre and 5, 10, 15, 20, 25, and 30 minutes after salve application			X	X
Estimated time to complete	20 min	45 min	85-90 min	85-90 min

Figure 3: TcPO2 sensor placement



Results

Sixteen participants were recruited and retained in the trial. No allergic reactions or clinically significant adverse events occurred during the clinical trial.

The primary outcome, mean *between* condition difference in TcPO2 in the leg sensors at 30 minutes, did not reach statistical significance:

TcPO2_{30mins} OHS - TcPO2_{30mins} Base = -0.39 +/- 8.54, p=0.86

The secondary outcome, mean *within* group difference in TcPO2 in the leg sensors at 30 minutes, for the OHS salve did reach statistical significance:

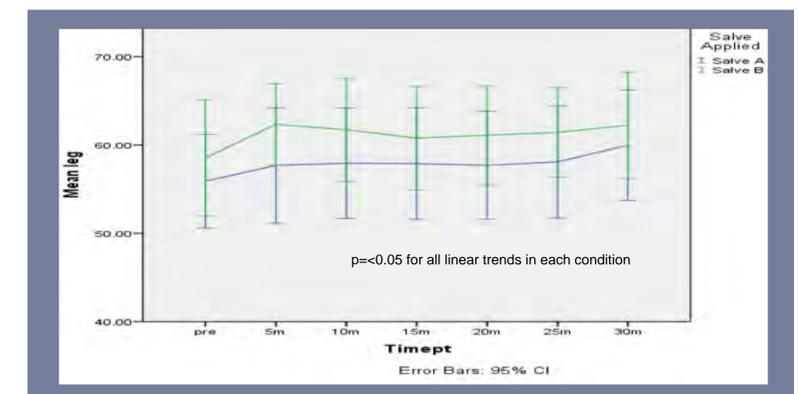
TcPO2_{30mins} OHS - TcPO2_{pre} OHS = 3.70 +/- 6.62, p=0.04

Repeated-measures analysis showed that there were significant linear trends for Time point, when considering Sensor 1 (p=0.005), Sensor 2 (p=0.008), or the Leg composite measure (see Figure 4, p=0.003). There were significant cubic time trends for all six sensors/composites (Sensor 1: p=0.032; Sensor 2: p=0.002; Sensor 3: p=0.01; Sensor 4: p=0.02; Leg: p=0.004; and Foot: p=0.01). The significant linear trends for the leg sensors confirm the results of the paired t-tests, that showed increases in TcPO2 over time, with either salve. The cubic trends are reflective of a pattern, shared by all sensors, in which there is an initial rise, a leveling off or decrease, then another rise towards the end of testing.

Conclusions

The Puremedy® Original Healing Salve increased TcPO2 after 30 minutes in people with type 2 diabetes, however the contributions of the herbal and homeopathic ingredients remain unclear.

Figure 4: Time trends in TcPO2 in Test and Control Salves



Acknowledgements & Disclosures

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