

A Pilot Study of the Antibacterial Activity of Topical Fatty Acids

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INTRODUCTION

Bacterial biofilms have been found in most chronic wounds and are believed to be the source of on-going inflammation. Most antimicrobial treatments have limited effects and are known to be cytotoxic. Approaches which either physically remove or use physical chemistry mechanisms have begun to show promise. Another line of possible treatment which is emerging is targeting of the bacteria's metabolism. In the wound, bacteria primarily metabolize sugars and proteins, but little is known about their lipid metabolism. We have begun to investigate a topically applied oil which may have both physical/chemical removal and antibacterial metabolism-based activities.

Hypothetical Modes of Action

- The oil may disrupt the bacterial membranes.
- The oil may “embargo” the bacteria, cutting them off from water and nutrients.
- The oil may cause the bacteria to change its method for seeking nutrients away from sugars and proteins and more toward fats.
- The oil may dislodge the bacteria off of the surface of the wound extracellular matrix/wound surface.
- The oil may be a barrier to external contamination.

The first step we took was to see if ANY effect occurs independent of understanding the mechanism. The experiments described herein sought to determine if the oil-based product could reduce viable *S. aureus* in a porcine skin wound model

METHODS

An ex vivo porcine skin explant model was used to establish a functional *S. aureus* biofilm for 5 days. The wounds were then treated with either an oil or with moistened gauze. The wounds were re-treated daily with either oil or more saline. Six explants per day from each group were harvested and viable total bioburden and biofilm were assessed.

After the initial results, the experiment was run again with the added step of first soaking the explant in phosphate buffered saline with 0.05% Tween 20 in order to see if the oil was masking the bacteria

RESULTS

At Day 0, the average bioburden was 4.8 log₁₀ CFU/ml with 3.64 log₁₀ CFU/ml of biofilm. After Day 1, total bacterial levels in the oil treated sample were reduced to 1.8 log₁₀ CFU/ml while the control increased to 9.0 log₁₀ CFU/ml. The levels of the oil-treated samples remained low and the control remained high every day thereafter.

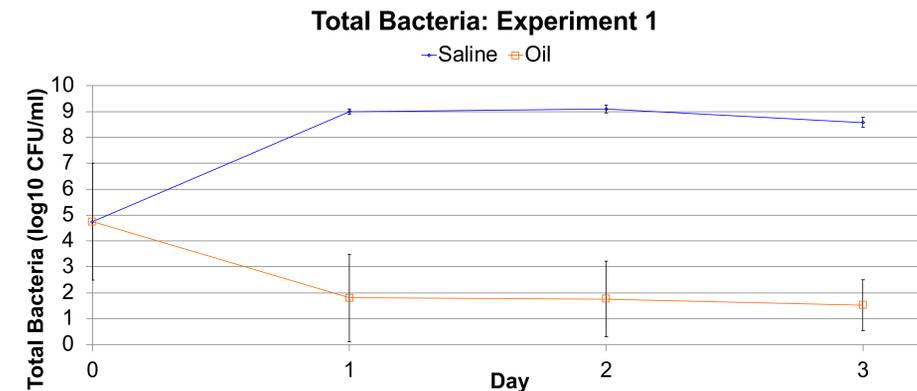


Fig 3. The results from the first experiment showed a large reduction which was very highly significant ($p \leq 1.1 \times 10^{-6}$).

After such a dramatic effect, we sought to replicate it. Also, since there was a significant effect on the total bacteria, we sought to see if there was also an impact on bacterial biofilms.

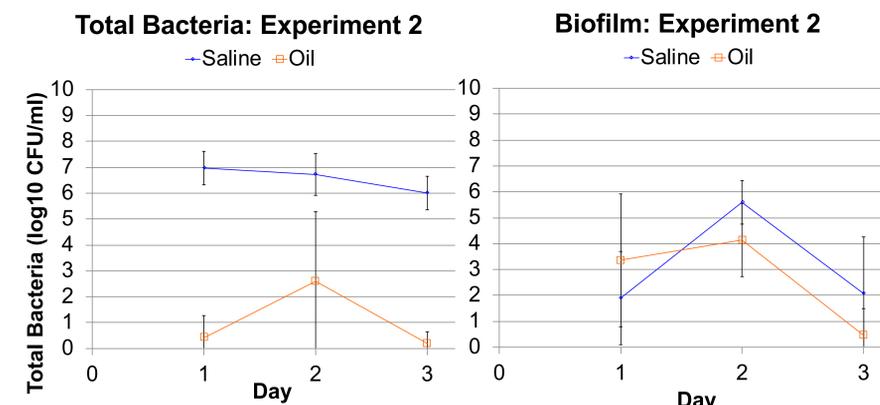


Fig 4. A) In the second experiment, a similar pattern was seen though the absolute numbers differed, and Day 2 was less consistent. The p-value was still significant with Day 2 having the highest p-value of $p = 0.01$. B) The viable biofilm counts contradict the total counts.

RESULTS CONTINUED

Oddly, the biofilm numbers did not change, contradicting the total bioburden results. Another experiment was performed and the total bioburden was reassessed using the 24 hr incubation period used for the biofilm assessment without antibiotics to determine if the incubation period caused the disparity. The total levels still remained around 1.0 log₁₀ CFU/ml; showing that the incubation period did not contribute to additional growth.

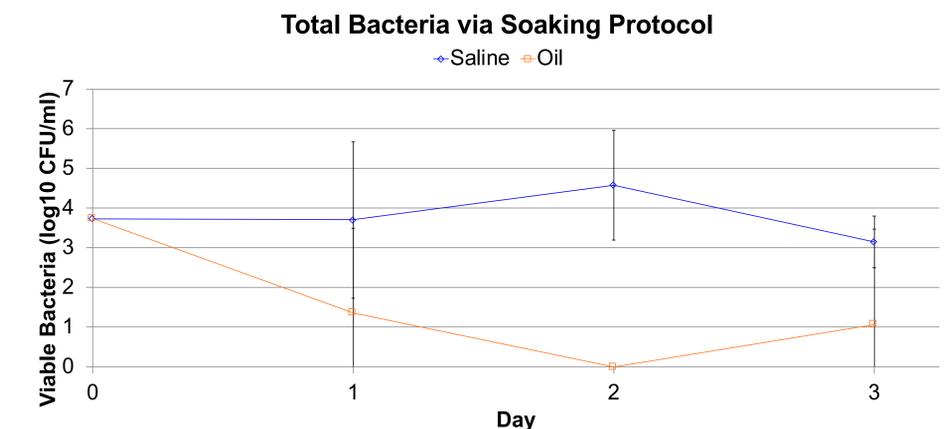


Fig 5. The results from a 3rd experiment which subjected the samples used for total bacteria quantification to the same incubation period as the the biofilm. The positive effect of the oil-based product still persisted; though the total viability of the saline-treated samples was decreased.

DISCUSSION

The immediate results from the total bioburden assessment are exciting, but still not certain due to the results seen for the biofilms. An imaging-based study to directly visualize the biofilm has begun and will be used to clarify the ambiguity. These results are very exciting given the potential for a nutritive pro-healing oil to also have an antibacterial activity. The additional experiments will determine if the current results stand and additional work in animal model or human trials are warranted.

CONCLUSIONS

- The initial reductions are promising.
- The oil might interfere with the standard porcine skin assay.
- At least 5 mechanisms of action are plausible and are under study.
- Alternative techniques are being used to validate these findings.

