Improving Skin Barrier Function During the COVID-19 Era: Laboratory Studies of a Prescription Tri-lipid Emollient

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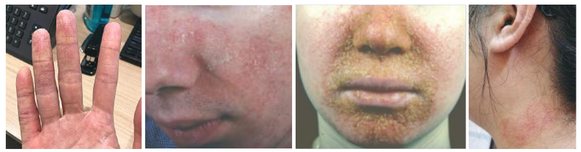
Synopsis

- Personal Protective Equipment (PPE), handwashing and sanitizers cause skin disorders in up to 63% of healthcare workers[1] raising interest in topical agents that enhance skin barrier function.
- Subject protocols were designed to evaluate the barrier function of Rx medical device creams with in vitro tests.
- A dye test found a Rx tri-lipid emollient was twice as effective as a Rx dimethicone.
- The tri-lipid emollient also blocked microbial passage through a filter barrier test.
- Clinical studies are warranted to demonstrate potential benefits of Rx lipid-based emollients to improve skin barrier function in the COVID-19 era.

Introduction / Objective

Personal Protective Equipment (PPE) and stringent hygienic practices of this COVID-19 era often cause skin irritation, cracks, dryness, irritant contact dermatitis & other lesions, and raise concerns about skin colonization, nosocomial infections, safety and compliance of personnel because of compromised skin barrier function. Up to 63% of healthcare workers are affected by such skin disorders.[1] A recent study of 270 healthcare workers caring for COVID-19 patients in an Irish hospital found that 82.6% had dermatitis.[2] Among these frontline workers, 45% denied using emollients.

The objective was to evaluate the barrier function of Rx medical device creams with in vitro laboratory tests. That is, determine if medical device creams can enhance barrier function.



Pictures Sourced From: Lee H.C., Goh C.L. Occupational dermatoses from Personal Protective Equipment during the COVID-19 pandemic in the tropics – A Review. *Eur Acad Derm & Ven*. 2020 In press.
Gouin J-P, Kiecolt-Glaser JK. The Impact of Psychological Stress on Wound Healing: Methods and Mechanisms. *Immunol Allergy Clin North Am*. 2011;31(1):81-93.

Materials

- The first skin barrier protection product was Rx tri-lipid emollient EpiCeram®
- Comparator product was a dimethicone prescription cream commonly used in U.S. hospitals.
- 12-layer gauze was 2 x 2 inch Equate™ Gauze Pads used in dye-test.
- Whatman No. 5 Filter Paper with average pore size of 10 microns used in microbe test.
- 2 Gram (+) bacteria, *Staphylococcus aureus* and *Staphylococcus epidermidis,* and 2 Gram (-) organisms, *E. coli* and *Serratia marcescens;* 2 motile and 2 immotile species. Some are skin-related microbes.

References
1. Lee H.C., Goh C.L. Occupational dermatoses from Personal Protective Equipment during the COVID-19 pandemic in the tropics – A Review. *Eur Acad Derm & Ven*. 2020 In press. **2.** Kiely LF, Moloney E, O'Sullivan G, Eustace JA, Gallagher J, Bourke JF. Irritant contact dermatitis in healthcare workers as a result of the COVID-19 pandemic: a cross-sectional study. *Clin Exp Dermatol*. Published online July 23, 2020. doi:10.1111/ced.14397 **3.** Kitchel B. Performance Claims and Supporting Test Methods, a subsection of General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee. Published online September 20, 2016:37–55.

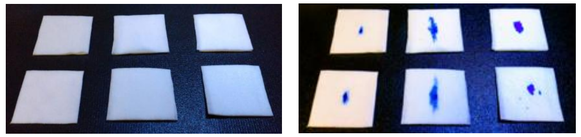
Disclosure: All authors are paid consultants, and the work was supported by Primus Pharmaceuticals, Inc

Method: Principle & Enhanced Barrier Dye Drop Test

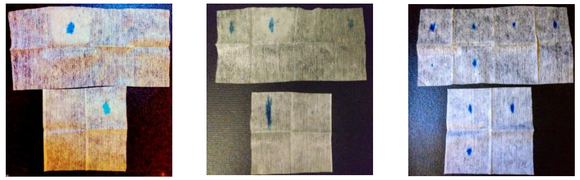
- PRINCIPLE. Standard Protocols used by the FDA to substantiate wound dressing barrier function[3] were adapted to evaluate the physical barrier effects of skin creams. Per these protocols, there are two key tests of in vitro barrier function: one uses dye and the other uses microbes to see if they can pass through a barrier dressing. In the case of dye, the variable of treating gauze with creams was added, and for the microbial test barrier gauze was replaced by filter paper.
- Matrices of sterile gauze or filter paper were treated with creams or not, either freshly applied or allowed to dry for 2 hours at 30°C.
- Dye Drop Test. For challenge of gauze by dye, 25 µLs of 1% aqueous methylene blue were applied, allowed to soak through the gauze for 30 minute, and the number of layers stained were photographed and counted.
- **Interpretation:** Dye penetrating fewer layers represents greater barrier function (protection).

Illustration of the "Dye Drop Test" used to demonstrate the blocking function of a barrier wound dressing (B).

Results: Enhanced Barrier Dye Drop Test

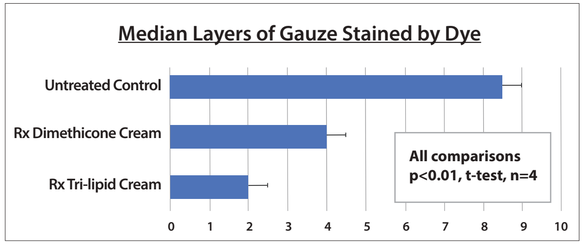


Sterile 2" x 2" gauze was treated with tri-lipid, comparator product, or nothing. Dye was added & soaked for 30 min. Then gauze was opened and photographed.



Tri-lipid | Comparator Product | Untreated Control

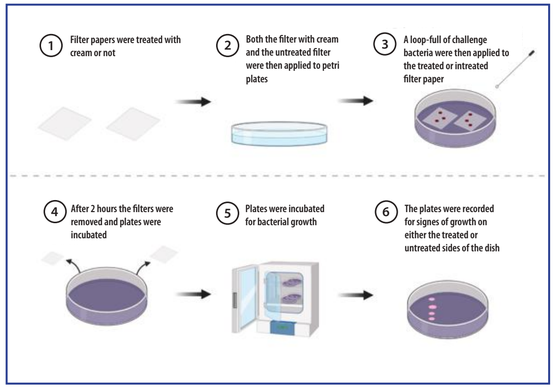
RESULTS: Untreated control gauze had the most stained layers & tri-lipid cream had the fewest layers stained. Dimethicone comparator differed from the others.



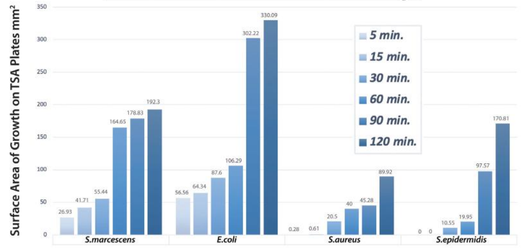
Method: Microbial Barrier Filter Test

- **Part 1 Goal.** Determine how much time is sufficient to allow microbes to move through a porous filter paper matrix and reach the surface of an agar plate.
- **Step 1.** Filter paper was placed onto agar ensuring no air was trapped. The filter was thoroughly wetted by the agar medium and warmed to 30°C.
- **Step 2.** At different times (t minus 2 h, 1.5 h, 1 h, 0.5 h, 15 min & 5 min) a standardized loop-full amount of each microbial species was placed on top of the filter paper. Counting down, at time zero the filter paper was removed ending the transit of any other microbes to the surface of the agar.
- **Step 3.** The plates were incubated at 30°C x 36 h. Microbes that passed through the filter paper grew into a mass of confluent colonies. This biomass area was measured.
- **Analysis.** SketchAndCalc (iCalc Inc.) was used to calculate the surface area of growth. Semi-quantitatively, the area is proportional to the numbers of microbes that passed through the filter paper, and this time dependence was determined.
- **Part 2 Goal.** Next, determine whether a cream can make the filter paper impervious to the passage of microbes.
- **Step 1.** Filter paper was cut into half circles. For treated filter paper, cream was applied and spread uniformly using a glass slide and dried for 2 h at 30°C. Untreated filter paper was used as a control.
- **Step 2.** Filter papers were placed onto agar and microbes were added as before. After incubation for 2 h at 30°C, the filter papers were removed.
- **Step 3.** The plates were incubated at 30°C x 36 h. Microbes that passed through the filter paper grew into a mass of confluent colonies. Plates were photo-graphed and results were recorded.
- **Interpretation:** No growth is proof of complete blockage of microbial passage through treated filter papers. Such a result was scored as PASSING the microbial barrier filter test.

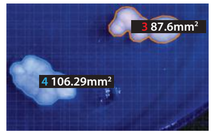
Illustration Of Microbial Barrier Filter Test



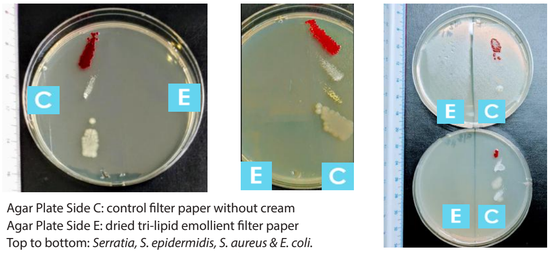
Results: Microbial Barrier Filter Test – Part 1



- Measured biomass area is related to time of exposure of microbes on filter. The motile species penetrated faster than immotile species.
- 30 minutes of exposure to the untreated, control filter paper was sufficient for all tested species to reach the agar surface.
- Providing exposures of 90 minutes to 2 hours assured a good challenge of barrier function of applied creams.



Results: Microbial Barrier Filter Test – Part 2



Agar Plate Side C: control filter paper without cream
Agar Plate Side E: dried tri-lipid emollient filter paper
Top to bottom: *Serratia, S. epidermidis, S. aureus & E. coli.*
RESULT: Tri-lipid PASSES microbial barrier filter test repeated 4 times

Conclusions

- Limitations. Variety of microbes & creams tested were limited.
- These in vitro experiments demonstrate that a prescription tri-lipid emollient provided a physical barrier to passage through matrices when challenged by methylene blue dye and four different microbes.
- The proprietary 3:1:1 tri-lipid emollient had twice the barrier function as a common hospital prescription dimethicone cream in the in vitro Barrier Dye Drop Test.
- Clinical studies are warranted to demonstrate potential benefits of Rx lipid-based emollients to improve skin barrier function in the COVID-19 era.
- Readily available methods are shown to evaluate barrier function of skin creams in vitro, and positive findings are timely during the COVID-19 pandemic.