In vivo methods to evaluate a new skin protectant for loss of skin integrity

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ABSTRACT

A new skin protectant was developed for use on conditions involving partial-thickness skin loss such as severe incontinence-associated dermatitis. This new formulation is based on a cyanoacrylate chemistry designed to polymerize in situ and create a breathable film able to protect the skin surface from external irritants. This film provides an environment favorable for healing to occur beneath the film. To evaluate the characteristics of the novel chemistry, we devised a preclinical testing strategy comprising three different animal models. The data from all three models was considered collectively to create an overall assessment of effectiveness. A guinea pig model was used to evaluate the barrier efficacy of the new product in protecting intact skin from irritation. A porcine partial-thickness wound model was used to evaluate the efficacy of the product in helping control minor bleeding and exudate. A similar model was also used to assess the process of reepithelialization in the continued presence of an irritant. In the first model, untreated sites had 8.5 times more irritation than sites covered with the new product ($p < 0.001$). In the second model, a single application of the new product successfully attached to intact peri-wound skin and to denuded, weepy skin. It significantly reduced the amount of fluid weeping from the wounds ($p \leq 0.001$) and continued to perform throughout a 96 hours experiment. In the third model, the percent of reepithelialization was significantly greater for the wounds covered with the new product than for the control wounds ($p = 0.003$; on average, 18.3% greater, with a 95% confidence interval of 9.2% to 27.5%). These results suggest that the new skin protectant protects intact and denuded skin from irritants and provides an environment favorable to healing, offering promise for the management of various conditions involving loss of epidermis.

Wound healing is a complex biological process with several steps involved to restore skin integrity (hemostasis, inflammation, granulation tissue formation, and remodeling). The biological events involved and how they can be modulated using current knowledge and technology have been recently reviewed by Wong et al.[1] The context of the wound impacts the sequence of events that will follow and the successful resolution of the wound. A variety of products are available to manage wounds. Dressings are typically used for acute (surgical or traumatic) and chronic wounds (recently reviewed by Sood et al.[2]); however, severe skin damage such as that seen in incontinence-associated dermatitis (IAD) requires a different approach due to the location on the body and the necessity for frequent cleaning caused by incontinence episodes. In mild cases of IAD (skin is red and macerated but epidermis is still present), barrier films can be used. These products are applied as liquids, either in a spray formulation, a wipe, or a wand applicator, and polymerize to form a film in situ and protect the skin. In severe cases of IAD, however, the epidermis is breached and the resulting partial-thickness wounds produce exudate, which prevents such barrier films from adhering to the skin. In this case, clinicians typically resort to barrier products including ointments and pastes to provide protection to the skin.[3] IAD can present with varying degrees of severity, from erythema to epidermal denudement, which is equivalent to a partial-thickness wound. The treatment modalities should take into account the specific needs of the wound and its environment, and factors such as patient age and coexisting morbidities. There is no universal product that will work on all wounds, and deciding which product to use depends on matching wound characteristics with product capabilities.

The purpose of this article is to describe a new skin protectant formulation and to propose an integrated preclinical testing strategy. The novel formulation is intended to manage IAD-related partial-thickness wounds by protecting the exposed deep epidermis or dermis from external irritants and allowing healing to occur beneath the protective layer. The denudement observed in severe cases of IAD is particularly challenging to manage because it often presents as multiple small open areas of irregular shape over a contoured body surface. These open areas are exudative and ointments and even many pastes do not adhere to the wet weeping surface. The damaged skin is constantly exposed

to moisture and irritants such as urine and feces in cases of continued incontinence. The skin is therefore at a greater risk for further breakdown and maceration, resulting in decreased skin integrity.[3–5] The technology presented here could conceivably be used also on other types of partial-thickness wounds or damaged skin, such as split-thickness skin graft donor sites, or severe peristomal skin damage.

Numerous animal models have been used to study wound healing and the selection of the most relevant model for a particular study is a critical decision. This topic has been well reviewed by Lindblad,[6] who concludes that researchers should make the best use of the wealth of approaches available to clearly answer the question at hand. Our approach has been to use three different animal models in parallel to assess the efficacy of a new product at protecting the skin from irritants, controlling exudate, and allowing reepithelialization. For the skin irritation aspect, we chose the hairless guinea pig, which has been shown to react in a similar pattern to human skin when exposed to skin irritants or composite skin-care formulations.[7] We included this to model the environmental conditions of incontinence using a simulated incontinence fluid. IAD is a particular area of research where we are not aware that any animal models have been proposed yet to test solutions. For exudate control and reepithelialization, we believe that partial-thickness wounds on pigs provide an appropriate model. The pig has been recognized for a long time as the species with the skin presenting most similarities to human skin.[8,9] For our purposes, a partial-thickness pig wound provides a good representation of the denudement observed in severe cases of IAD, not only from the wound reepithelialization standpoint, but also from the exudate management standpoint, which has not been studied and modeled in animals as extensively as the cellular healing mechanisms. We have therefore used all three models concurrently to test the new skin protectant formulation.

MATERIALS AND METHODS

Description of new formulation

The investigational product is a solution based on a patented acrylate chemistry, which forms a durable, transparent elastomeric barrier upon application to skin. The product is applied as a liquid to effectively cover the desired area and conform to the topography, and polymerizes in situ into a film within approximately 30 seconds. This film is breathable and capable of preventing irritants from reaching the skin surface. It remains intact even under conditions of continuous or repeated exposure. A customized acrylic polymer, combined with 2-octyl cyanoacrylate, creates the film structure. The film formers are delivered from a well-tolerated solvent. Figure 1 shows the applicator used to deliver the product to the skin surface.

Testing done prior to applying the product to animals included cytotoxicity, irritation, sensitization, genotoxicity, and systemic toxicity based on the criteria of expected use (>30 days in contact with a breached skin barrier) and guidance covering the biological evaluation of medical devices outlined in EN ISO 10993-1:2009. The results supported a conclusion that the product is safe for its intended use. In addition, the formulation forms a film when deposited on tryptic soy agar and prevents the proliferation of microorganisms seeded over the top in these in vitro conditions (assay done with a Gram-positive bacteria [*Staph aureus* ATCC 6538], a Gram-negative bacteria [*Pseudomonas aeruginosa* ATCC 9027], and a fungus [*Trychophyton rubrum* ATCC 28188]; data not shown).

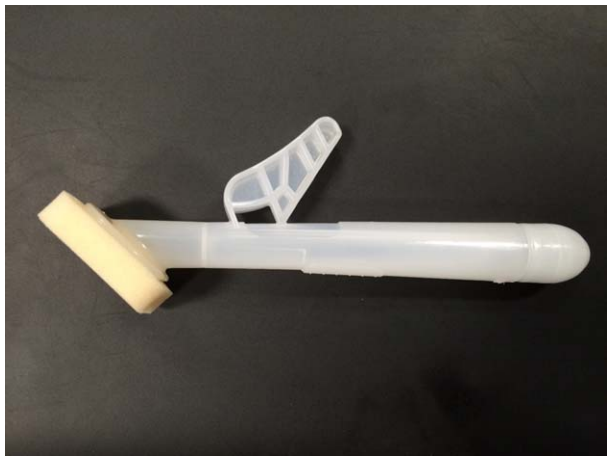

Figure 1. Applicator for the investigational product. [Color figure can be viewed at wileyonlinelibrary.com]

Animal models

The three studies described below were approved by our institutional animal care and use committee and animal care complied with the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act (9CFR).

Guinea pig intact skin model to evaluate protection from irritants (Model 1)

Intact skin (protected or not) was challenged with a caustic irritant and the degree of irritation after 48 hours was measured by clinical observation.

Twenty-four male hairless guinea pigs (Institute Armand Frappier, Montreal, Canada) were used in this model. The animals weighed 250–300 g at arrival and were 4–5 weeks of age. Due to the noninvasive nature of this protocol, animals were allowed to recover and could be reused with a rest period of at least 3 weeks between experiments. The skin was prepared with an antiseptic agent 24 hours prior to the experiment with a wash and wipe of isopropyl alcohol and then again immediately before use to remove excess oil from the surface of the skin. Prior to the procedure, animals were placed under general anesthesia maintained with inhalational isoflurane. On each guinea pig, six 1.5 by 1.5 inch sites were symmetrically marked on the sides, three on each side of the spine. The investigative product was applied to five sites with a saturated foam swab. One site was left untreated and served as an internal control. In this model, development formulations were tested in parallel with the final formulation. We only report here the results on the final formulation, with $n = 58$. All sites were allowed to dry for 5 minutes. Each site was challenged with an alkaline fluid simulating an irritant

Table 1. Irritation assessment scale used in Model 1

Score	Observation
0	Clear skin with no signs of erythema
1	Almost clear; slight redness
2	Mild erythema, definite redness
3	Moderate erythema; marked redness
4	Severe erythema; fiery redness

(pancreatin, 1 g/100 mL, in 0.05M potassium phosphate solution adjusted to pH 9) by pipetting 0.50 mL of fluid into the cotton padding of a Hill Top Chamber and placing it on the site. The sites were then covered with 3M Tegaderm HP Transparent Film Dressing (3M, St. Paul, MN), custom cut to size. After 48 hours, the dressings were removed and the sites were graded on the amount and severity of skin irritation using the Clinician Erythema Assessment scale (score of 0–4, see Table 1) described by Tan.[10] The amount of irritation was measured as a percentage of the 25 mm^2 round area of challenge given by the Hill Top Chamber. On two guinea pigs, the Hill Top Chamber on the control area was no longer adherent at 48 hours. The data from those two animals were omitted from the analysis (leaving a N of 22 for controls).

Statistical analysis

This study sample size had at least 90% power to detect a difference of 1 in mean skin irritation score, assuming a standard deviation of 0.6. Statistical evaluation was done on the normalized skin irritation scores at 48 hours. The scores were normalized by multiplying each score by the estimated percent of area involved. For example, if a site had a score of 2 over 50% of the site, the score was $2 \times 0.5 = 1$. The two treatment groups compared were untreated sites and sites coated with the investigative formulation. The scores were compared using an analysis of variance (ANOVA) with guinea pig as a random effect and formula (investigative formulation or untreated) as a fixed factor in the model. p-values ≤ 0.05 were considered significant.

Porcine partial-thickness wound model to evaluate the control of minor bleeding and exudate (Model 2)

Wound exudate was measured by collecting and weighing fluid from wounds both immediately after formation and again after 96 hours.

Six female Yorkshire domestic pigs (Midwest Research Swine, Gibbon, MN), 30–32 kg, 8–10 weeks of age, were used in this model. The animals were acclimated for 1 week and fasted overnight prior to the experiments. The protocol was approved by the 3M IACUC. Each pig was anesthetized and maintained under general anesthesia with inhalational isoflurane. The hair on the dorsum of the animals was clipped and shaved, and three washes of isopropyl alcohol and betadine surgical scrub were applied to the skin prior to incision. The experiment was conducted in a fully sterile environment inside a sterile field. On each pig, ten 2 by 2 inch sites were symmetrically marked on the back, five on each side of the spine. Partial-thickness wounds were created using an electric dermatome (Slimline Model S, Integra Life Sciences, Plainsboro, NJ) set to 0.5 mm thickness. After each wound was created, a nonwoven gauze pad was applied over the site with pressure provided by a sterile, gloved hand for 5 minutes in order to reduce the amount of immediate wound drainage. After the 5 minutes of pressure, the wounds were randomized in their designated treatment group (investigative product, $n = 48$ or untreated control, $n = 12$). The investigative product was applied to the treated wounds using a custom-designed foam applicator. To maintain consistency for all wound sites, control sites were subjected to the same applicator procedure as treated sites, but without applying the test product. This avoided potential bias of wound fluid absorption by the foam applicator in contact with the wound site. The sites were then allowed to rest for 5 minutes in order to ensure the treatment group was dried. A preweighed gauze pad was placed over each wound and held in place with a sterile gloved hand for 15 seconds to absorb all fluid weeping from the wound. The gauze was held over each site with the palm of the hand to ensure even pressure. The weight of the gauze was measured and recorded to calculate the amount of fluid absorbed from each wound. Following this, 3M Steri-Strip Compound Benzoin Tincture (3M) was painted between the wounds and on the surrounding area to increase adhesion of dressings and each wound was covered with a preweighed 3M Tegaderm Foam Non-adhesive Dressing (3M) to absorb exudate and provide padding protection to the wounds. The dressings were secured with 3M Veterinary Elastic Adhesive Tape (3M), after protecting the skin to be taped with 3M Cavilon No Sting Barrier Film (3M). All animals were followed for 96 hours. Any changes in eating, drinking, and movement were observed and recorded. If needed, additional pain relief was given based on veterinary recommendation. After 96 hours, all the foam dressings were removed and weighed to calculate the amount of wound exudate collected.

Statistical analysis

This study sample size had at least 90% power to detect a difference of one standard deviation in mean fluid absorbed. Statistical evaluation was done on the amount of fluid collected post wound creation (T0) with the gauze pads and after 96 hours with the foam dressings. The total fluid weights were compared using an analysis of variance (ANOVA) with Yorkshire pig as a random effect and treatment (investigative formulation or untreated control) as a fixed factor in the model. p-values ≤ 0.05 were considered significant.

Porcine partial-thickness wound model to evaluate reepithelialization in presence of an irritant (Model 3)

Wound reepithelialization was measured on histology sections at 96 hours.

Seven female Yorkshire domestic pigs (Midwest Research Swine), 30–32 kg, 8–10 weeks of age, were used in this model. The method used to make the wounds was the same as described above in Model 2. After the 5 minutes of pressure, the wounds were randomized in their designated treatment group (investigative product or

untreated control, $n = 35$ for each). The investigative product was applied to the treated wounds using a custom-designed foam applicator. The sites were then allowed to rest for 5 minutes in order to ensure the treatment group was dried. All sites were challenged with a caustic (alkaline) fluid simulating an irritant such as incontinence fluid (same as used in Model 1), by pipetting 0.50 mL of the pancreatin solution into the cotton padding of each of four Hill Top Chambers[11] placed on the wounds. 3M Steri-Strip Compound Benzoin Tincture (3M) was painted between the wounds and on the surrounding area to increase adhesion and each wound was covered with 3M Tegaderm Foam Non-adhesive Dressing (3M). The dressings were kept in place with 3M Veterinary Elastic Adhesive Tape (3M), after protecting the skin to be taped with 3M Cavilon No Sting Barrier Film (3M). All animals were followed for 96 hours. Any changes in eating, drinking, and movement was observed and recorded. If needed, additional pain relief was given based on the veterinary recommendation. After 96 hours, the foam dressings were removed, the wounds imaged, and the animals were euthanized. Two samples from each wound were immediately excised for histological evaluation from the area where the Hill Top Chambers were placed. The excised samples were approximately 0.5 by 2.2 inches and were taken slightly past the wound margin. They were immersed in formalin and sent to an independent lab (Marshfield Labs, Marshfield, WI) for processing and histopathology interpretation by a veterinary pathologist blinded to the treatment code. The fixed samples were embedded in paraffin, stained with hematoxylin-eosin, and evaluated for percent reepithelialization using the formula: ([cumulative length of reepithelialization/length of wound]$\times$100), calculated from the measurements taken on histology sections. This is similar to a method described by Peura et al.[12]

Statistical analysis

This study sample size was chosen to have at least 90% power to detect a difference of 15% in mean percent reepithelialization, assuming a residual standard deviation of 15%. The data were analyzed using a mixed model analysis of variance, with treatment group as a fixed factor in the analysis, and pig and pig-by-treatment group as random factors. p-values ≤ 0.05 were considered significant.

RESULTS

Guinea pig intact skin model to evaluate protection from irritants (Model 1)

The skin irritation score was assessed at 48 hours using the scale described in Table 1. Figure 2 shows an example of the data obtained with this model.

The average normalized irritation score was 0.2 for the test product and 1.7 for the untreated control (Figure 3). From the ANOVA model, the difference between treatment groups was statistically significant ($p < 0.001$).

These results indicate that the investigative formulation was able to significantly reduce skin irritation in the presence of a caustic irritant and continued to perform throughout the 48 hour experiment after a single application. The untreated sites had 8.5 times more irritation than sites covered with the test product.

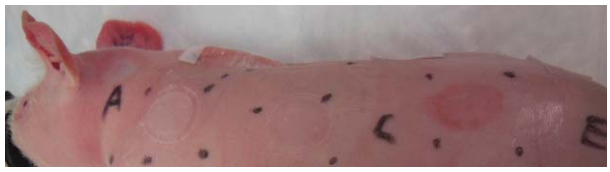

Figure 2. Example of guinea pig skin irritation experiment (Model 1). Sites A and C were treated with the investigational product; site E was the control.

Models 2 and 3 both used the same type of partial-thickness wounds on pigs but measured different outcomes. Figure 4 illustrates the visible effect of the investigational product on this type of wound at the time of application.

Porcine partial-thickness wound model to evaluate the control of minor bleeding and exudate (Model 2)

The amount of wound exudate was measured by collecting and weighing fluid from wounds immediately post creation and after 96 hours. The replicates for total fluid weight were averaged and the differences between the treatment groups were calculated. Figure 5 shows the mean weight of fluid absorbed with gauze immediately after wound creation, and Figure 6 displays the mean weight of fluid absorbed with the foam dressings after 96 hours. The difference between treatment groups was significant at both time points ($p = 0.001$ at each time point).

Post wound creation (T0), wounds treated with the investigative formulation produced an average of 0.083 g of wound fluid compared to 0.238 g for untreated wounds. The untreated wounds had 2.9 times more fluid weeping from them after 15 seconds than wounds covered with the test product. This fluid was red and composed of exudate mixed with a small amount of blood.

After 96 hours, wounds treated with the investigative formulation had produced an average 2.231 g of wound fluid since T0 compared to 4.328 g for untreated wounds (control). The untreated wounds had 1.9 times more fluid weeping from them after 96 hours than wounds covered

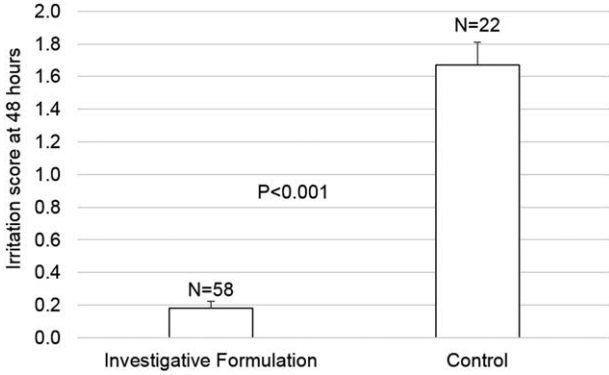

Figure 3. Mean skin irritation scores at 48 hours after caustic challenge in guinea pig intact skin model.

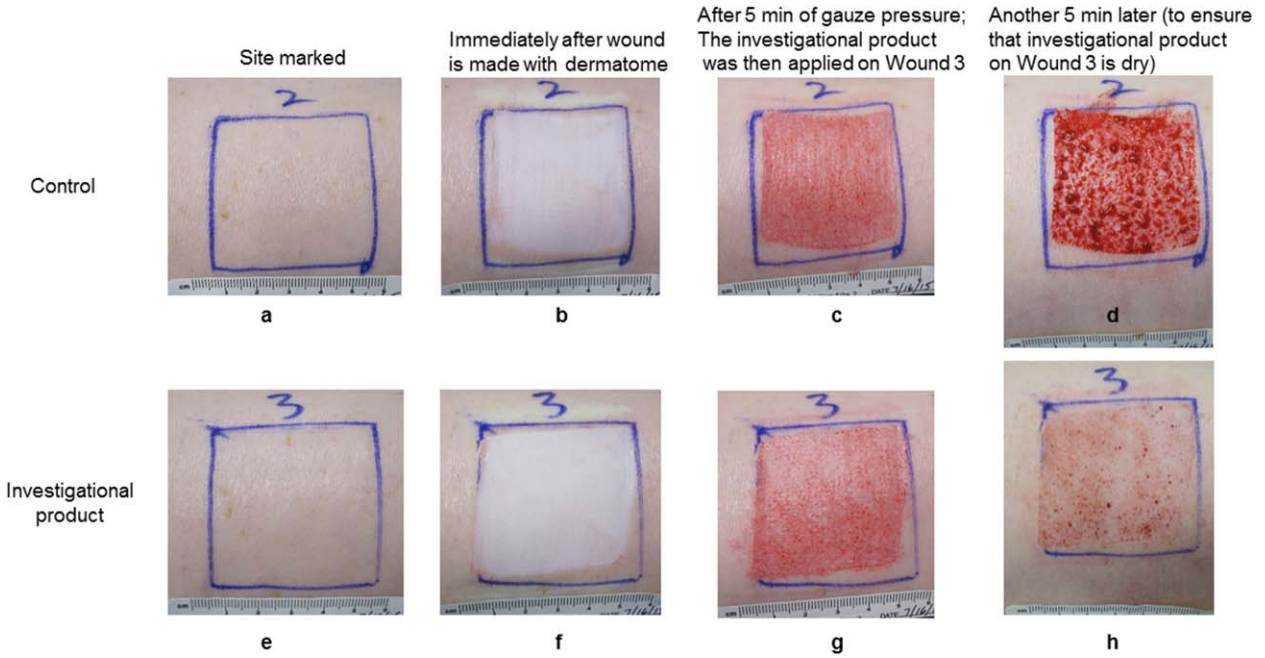

Figure 4. Example of pig partial-thickness wounds experiment (Models 2 and 3). The effect of the investigational product on reducing exudation was visible within minutes of application.

with the test product. This fluid was dark (due to blood oxidizing over time) and obviously contained some amount of blood mixed in with the exudate.

These results indicate that the investigative formulation helped reduce the amount of minor bleeding and weeping from wounds compared to untreated wounds and that this effect could last at least 96 hours. The new formulation is expected to serve a similar function clinically, potentially reducing the fluid that can lead to maceration.

Porcine partial-thickness wound model to evaluate reepithelialization in presence of an irritant (Model 3)

The percent reepithelialization was measured on histological sections at the end of 96 hours. The replicates were averaged and the difference between the treatment groups was calculated. The difference between treatment groups was significant ($p = 0.003$, Figure 7).

The least squares estimates of the mean (SE) percent reepithelialization for the investigative formulation was 80.6% (5.7%) compared with 62.2% (5.7%) for the untreated group. On average, the test formulation had 18.3% greater reepithelialization than untreated, with a 95% confidence interval of 9.2 to 27.5%. Wounds treated with the test formulation had consistent, continuous, long stretches of reepithelialized epidermis which frequently displayed elongated rete pegs similar to the native epidermis (Figure 8). Untreated tissues had reepithelialized epidermis that was variable in quality, less linear, more disorganized and frequently surrounded by white refractile foreign material associated with inflammation.

These results indicate that the investigative formulation provided a barrier to the simulated incontinence fluid as

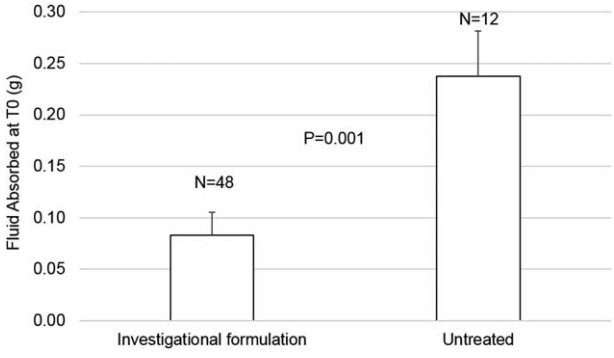

Figure 5. Mean weight of fluid absorbed with gauze immediately after wound creation in porcine partial-thickness wound model.

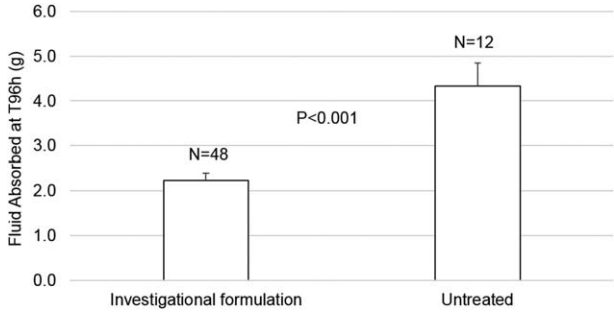

Figure 6. Mean weight of fluid absorbed with gauze 96 hours after wound creation in porcine partial-thickness wound model.

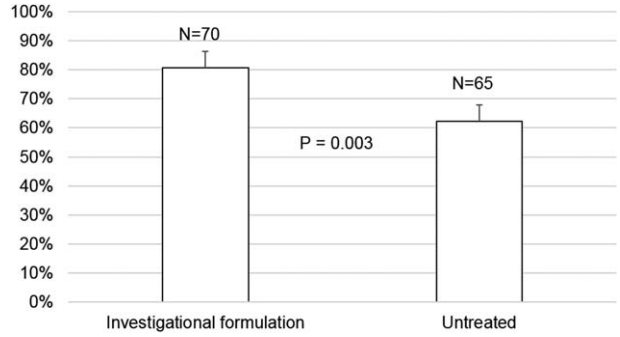

Figure 7. Mean percent wound reepithelialization at 96 hours (with standard errors) in porcine partial-thickness wound model. Since two samples were taken for each wound, $n = 70$ for the investigative formulation. Five samples are missing from the untreated control group ($N = 65$) because the wound margins were not available on those samples and the pathologist did not interpret those sections.

reflected in the significantly greater amount of reepithelialization in the wounds receiving the test product compared to control wounds after 96 hours. The new formulation is expected to serve a similar function clinically, providing a barrier that allows the natural process of reepithelialization to occur even in the presence of a caustic insult and/or excess fluid.

DISCUSSION

Using three different animal models in parallel, we have evaluated the effectiveness of a new skin protectant formulation at protecting the skin from irritants, controlling exudate, and allowing reepithelialization. Our results show that this novel formulation can reduce irritation in intact skin subjected to an irritant, reduce the amount of minor bleeding and weeping from partial-thickness wounds for at least 96 hours, and allow for greater reepithelialization at 96 hours in partial-thickness wounds subjected to an irritant.

The guinea pig model was selected as an accepted model for contact dermatitis.[7] The porcine model was selected because of the anatomical and physiological similarities to human skin,[9] making it suitable for evaluating formulations designed for use on human wounds. Numerous studies have been published using such models to characterize the healing process for various types of wounds (e.g., partial-thickness, full-thickness, and incisional wounds) and to evaluate the effects of various products on healing[12–16] or the irritant potential of various substances on skin.[17,18] Other animal species have also been used as models for wound healing studies, such as mice, rats, and rabbits.[19–22] Kruse et al.[23] have reviewed many animal models to discuss the major role played by the external microenvironment of a wound (temperature, hydration, oxygen content, pH, and microbial load) in the healing process.

There is very limited literature to our knowledge on animal models used specifically to mimic IAD. One group however has used a rat model along with a model in human volunteers to study skin maceration. They reported on the ultrastructural alterations they observed, as well as on the fact that maceration disrupted the skin barrier function.[24] Their study also demonstrated that aging enhances skin maceration, suggesting that promoting skin barrier recovery after maceration is especially important in the elderly. These findings are relevant for skin challenged by urinary incontinence, since maceration is a consequence of continued exposure to excessive moisture. The same group published a separate study in which they used their rat model to study the histopathological changes caused by proteases and bacterial inoculation in skin maceration. Their description is believed to be the first showing the effects of proteolytic skin maceration on the tissue structure of the skin through macroscopic and microscopic observations.[25] These findings are important as the researchers added to their model proteases and bacteria, which are additional challenges brought on by fecal incontinence.

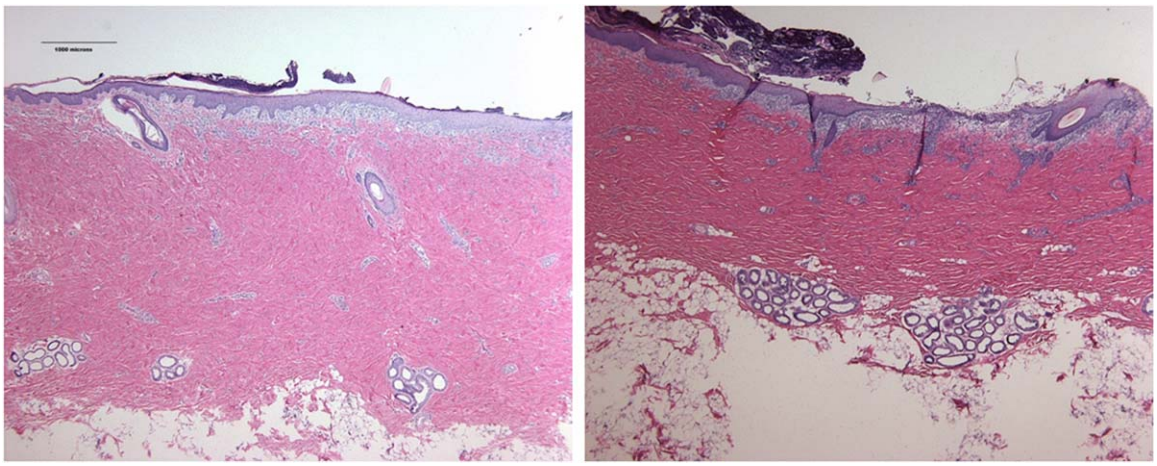

Figure 8. Hematoxylin-eosin stained histological sections of the area including the wound margin (partial-thickness wounds) at a 25× magnification (bar = 1000 μm). Left: wound treated with investigative formulation at 96 hours, right: control wound at 96 hours.

They propose the possibility that the histopathology of skin lesions caused by feces differs from regular dermatitis.[25] They have not, however, studied any products intended to manage these skin lesions in their model. This type of work has typically been done in humans and compared products already on the market.[26–28] Our work now offers a preclinical strategy to screen new formulations intended for this application.

Other types of partial-thickness wounds or damaged skin could conceivably benefit from this new technology, such as split-thickness skin graft donor sites or severe peristomal skin damage. In the case of split-thickness skin graft donor sites, there is a body of literature on clinical studies comparing various dressings for this application. A systematic review of 75 articles describing over 50 different dressings in studies published before 2008 concluded that there is no clear evidence of the superiority of wet dressings over dry ones as had been previously published.[29] Since then, multiple studies have compared different subsets of two or three dressings in randomized controlled trials, so it is still unclear whether one dressing is superior to all others.[30–35] In general, the difficulty associated with covering donor sites consists in satisfactorily achieving exudate absorption to avoid maceration, without drying the wound to the point of having the dressing adhere to it. Problems with leakage of blood and fluid are common,[35] and patients often complain more about the donor site than the site treated with the graft due to pain, irritation, and the discomfort caused by bulky or leaking dressings.[33] Better solutions are still needed for this application in order to manage the donor site with minimal dressing changes in order to reduce disruptions to the healing process. In fact, a recent study investigated the use of n-butyl cyanoacrylate to fix split-thickness skin grafts to the wound bed in a rat model and showed a reduction in the time needed for surgery and a higher graft survival rate.[36] Our study shows that the new skin protectant applied as a liquid that forms a film in situ might offer a potential solution to reduce the amount of exudate produced in the early stages of healing, or to serve as the main wound covering once the exudate production has sufficiently subsided. An ostomy is an intervention performed in patients with serious digestive diseases and refers to the surgically created opening in the body for the discharge of body wastes. Various appliances can be used to collect the discharge. These appliances need to adhere very well to the skin surrounding the orifice and they need to be changed periodically. Peristomal moisture-associated skin irritation is believed to be the most prevalent complication of this procedure, and it is associated with partial-thickness skin loss.[37] This skin condition, given its location near an orifice and the need to attach an appliance, does not lend itself to the use of dressings. Meticulous care of the site and the skin surrounding it is key to the prevention and treatment of this problem.[38] The new skin protectant presented here could conceivably provide an additional option to manage ostomy sites.

There are limitations to this study. In Model 1 (the guinea pig skin irritation model), we did not include a standard barrier film control. We reasoned that the efficacy of existing barrier films on intact skin has been proven already and that it would constitute an unnecessary use of animals. We felt that the new proposed formulation had to be proven in this type of model, but the work on existing barrier films would be superfluous because these products are already known to adhere well to intact skin and to work well in patients with simple urinary incontinence where the skin may be red and macerated but not denuded/weeping. In Models 2 and 3, existing barrier films could not be used because they do not adhere to wet, exuding skin. The standard of care for IAD with epidermal denudement is pastes (e.g., zinc oxide formulations). Those do not adhere very well to wet tissues either, but when enough paste is used, one can manage to cover the area. In the past we have run experiments using pastes in the same pig model, but because of the constraints of animal handling, those wounds had to also be covered over the paste with a foam dressing, otherwise the animals move and rub and the paste does not stay on for any length of time. For the current study, we believe that it was a cleaner comparison to use only a foam dressing for the control group, given that this resembles how non-IAD partial-thickness wounds are treated. Combining a paste and a foam dressing is not a treatment option that is commonly found in any clinical application and seemed less relevant.

In summary, the work we present here combines three models to study the separate aspects of managing exudate and protecting the skin to create an environment favorable for healing even in the continued presence of an irritant. We believe that this combination of models represents a valid approach to study new formulations intended for the restoration of skin integrity. Moreover, our results demonstrate that the new formulation is unique in its ability to be applied as a liquid and form a film that adheres to denuded skin, even in the presence of exudate. The data suggest that the investigative product protects intact and denuded skin from irritants and provides an environment favorable to healing, offering promise for the management of conditions involving loss of epidermis. This formulation has been recently tested in a clinical setting (submitted manuscript) on 16 patients suffering from IAD and showed promise for this indication. A larger scale study is under way, and other clinical studies for different indications will be needed to confirm the efficacy of this product for additional applications.

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Conflicts of Interest: All authors are employees of 3M. Deena Conrad-Vlasak is no longer an employee of 3M but she was when the work reported in this manuscript was performed. All authors have participated in the writing of this manuscript and no ghost writer was used to write this manuscript.

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