Topical Foam Formulations

Featuring:
- Review of Topical Drug Delivery
- Explanation of Foam Technology
- Clinical Applications of Foam Formulations

By Leon H. Kircik, MD and Joseph Bikowski, MD

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The Science of Topical Foam Formulations

Topical drug delivery remains the most common method for providing dermatologic therapy. Historically, it is associated with enhanced overall safety and minimal if any risk of systemic exposure and associated side effects. However, effective topical drug delivery presents challenges. Because the epidermal barrier is supposed to prevent entry of chemicals and noxious materials, it makes the passage of topically applied drugs difficult. Due to the efficiency of the epidermis in performing its function as a barrier, the amount of topical drug that gets through the stratum corneum is generally low, even with a well developed vehicle. For example, systemic absorption of corticosteroids through intact, non-inflamed skin is typically less than five percent of applied drug.

Topical drug formulators must develop topical drug delivery systems that efficiently bypass the barrier without significantly damaging the barrier. This presents a challenge. For example, harsh penetration enhancers could be used to significantly degrade the barrier and permit rapid diffusion of drugs.

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About the Authors
Leon H. Kircik, MD, Chair
Clinical Associate Professor of Dermatology
Mount Sinai Medical Center
Indiana University School of Medicine
Physicians Skin Care, PLLC; DermResearch, PLLC
Louisville, KY

Joseph B. Bikowski, MD
Clinical Assistant Professor of Dermatology
Ohio State University
Bikowski Skin Care Center
Sewickley, PA

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into the stratum corneum or deeper skin layers. However, this degree of injury would produce a sustained and undesirable disruption of the barrier function, setting the stage for inflammation, infection, and other sequelae and likely prolonging if not exacerbating the existing disease process. Therefore, alternative methods of drug delivery are needed. Acceptable methods of encouraging drug delivery include the use of low concentrations of desquamating chemicals like propylene glycol—also a solvent and humectant—to widen the intercellular pathways through which topically applied drugs may pass.

Hydration of the stratum corneum is another method of enhancing drug delivery. As epidermal cells swell, the aqueous/lipid ratios within the skin are altered, and the cells no longer resist mechanical shearing and stress forces. This facilitates the passage of molecules between epidermal cells. Additionally, hydration is suspected to potentially reveal drug binding sites and/or help to retain drug in the epidermal layers. Hydration also helps maintain normal desquamation or may encourage desquamation of the corneocytes and thus create passage ways that enhance penetration of a drug.

Hydrating or penetration-enhancing chemicals are just one part of the topical vehicle delivery system. As addressed in previous editions of Vehicles Matter (available online at VehiclesMatter.com), six primary considerations guide the development of a suitable topical drug vehicle. The vehicle must:

1. Efficiently deposit the drug on the skin with even distribution.
2. Release the drug so it can migrate freely to the site of action.
3. Deliver the drug to the target site.
4. Sustain a therapeutic drug level in the target tissue for a sufficient duration to provide a pharmacologic effect.
5. Be appropriately formulated for the anatomic site to be treated.
6. Be cosmetically acceptable to the patient.

**What Are Foams?**

The most common vehicle types (or more accurately dosage forms, by FDA nomenclature) used in dermatology are solutions, ointments, gels, creams, and lotions. A vehicle delivery system that is growing in popularity is foams. A foam is, quite simply, a dispersion of gas in a liquid or solid. While solid or dry foams exist within the medical marketplace (often as dressings), the focus of this discussion is liquid foams. It may be noted at the outset that the foaming action of liquid (gel, lotion) or solid (bar) cleansers is not relevant to this discussion of foams. However, cleansers can be formulated to be dispensed as foams.

Foams are colloids “composed of two or three distinct phases: a hydrophilic liquid continuous phase with a foaming agent, throughout which a gaseous dispersion phase is distributed. There may be a third hydrophobic dispersed phase.”

**Foams are colloids**

“composed of two or three distinct phases: a hydrophilic liquid continuous phase with a foaming agent, throughout which a gaseous dispersion phase is distributed. There may be a third hydrophobic dispersed phase.”

The type and amount of foaming agent will influence the stability of the foam and its density.

Most pharmaceutical foams are, strictly speaking, classified as liquid dosage forms, because that is how they exist in the can; The foam essentially is created at the time of use and exists only for a brief duration. Upon ejection, the propellant boils and diffuses while the foaming and bodying agents support the development of the crisp, white foam matrix. An emulsion in the can is converted to a foam and then back to an emulsion as the foam collapses. As Arzhavitina notes, “One should consider pharmaceutical foams as a ‘transition state’ between the

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**Vehicles Matter**

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device for foam generation, e.g. aerosol can, and the skin of the patient.7

Most foams used in pharmacological applications are aerosol foams, which typically come in two- or three-phase systems. Two-phase systems consist of a solution (solvent, foaming agent, foam stabilizer) and a gas phase comprised of propellant vapor. In three phase systems, typically the propellant is solved with a lipid phase that is emulsified in a water phase. A foaming agent and emulsifier (which may be the same chemical) are needed. The vapor phase is the third. Emollient oil-in-water (o/w) or water-in-oil (w/o) foams may contain no alcohol but may have lipid concentrations up to 75 percent. Waterless foams have also been developed that feature hydrophilic solvents, such as polyethylene glycol (PEG), propylene glycol, or glycerine.

Water is the most commonly used solvent in aerosol foams; ethanol and isopropanol are used less frequently. It is established that alcohols in a foam formulation can have a temporary permeabilizing effect on the skin prior to their evaporation, influencing drug delivery, as discussed below.5 Foams in general may be associated with enhanced drug penetration due to their unique nature. As volatile ingredients and co-solvents dissipate, a supersaturated drug formulation is transiently formed at the application site, and thermodynamic forces help drive active drug diffusion into the skin.5,9 A saturated solution may yield maximum concentration gradient and maximum thermodynamic activity, both of which facilitate rapid and efficient drug delivery and thus allow foams to potentially serve as an ideal topical drug delivery system.9

In addition to foaming agents, the product dispenser is essential to the creation of a topical foam. Aerosol packaging consists of three primary components: an aluminum or tin can (often coated on the interior with epoxide resins to prevent corrosion from solvents), a valve, and actuator. Valves can be metered for controlled dosing. Actuators, which may have specifically patterned aspirators, can modify the size and shape of bubbles formed in the foam and thus influence characteristics of the foam generated, including its volume and stability.7

Propellant technology is relatively complex and potentially expensive, which has been assumed to increase the cost of finished pharmaceutical foam products,9 however, cost effectiveness studies show certain foams may be no more expensive than alternative dosage forms when assessing the cost for treating similar surface areas.10 In one study, the foam equivalent of a fingertip unit (FTU) of a “conventional” formulation—cream, gel, lotion, or solution—was established, and the
comparable coverage rates were determined. The weight of an FTU of foam vehicle was determined to be 52.5 +/- 5.7 microg, and there were nine to 12 times as many FTUs in 100g of vehicle foam as in 100g of cream or gel. There were 2.3 to 2.8 times as many FTUs in vehicle foam as in 100g of lotion or solution. However, the study showed that the area covered by an FTU of foam vehicle was less than the area covered by an FTU of cream or gel. Nonetheless, the authors concluded that the total coverage area for 100g of foam was similar to that for 100g of other vehicle types.

Commonly used propellants include n-butane, isobutene, n-propane, or mixtures of these. These are liquefied under normal pressure, comprising three to 12 percent of the concentration of the initial formulation. Alternatively, systems can use compressed air as an immediately evaporating propellant. Sometimes, along with air, secondary propellants (n-pentane, isopentane, or isobutene) that have delayed evaporation are used. When these evaporate, they produce a cooling effect on the skin.

Various physical forces, often occurring simultaneously, may contribute to the breakdown of a foam once it is dispensed. In simplest terms, these forces involve the difference in air pressure between the air in the bubbles and air in the solution or ambient air (the gradient is higher in smaller bubbles), gravitational forces based on differing densities of the phases, and mechanical breakdown.

The type and amount of foaming agent affects the stability and density of the foam. Polymers such as cellulose and xanthan gum can be used to increase foam stability. The specific characteristics of the foam can be modified to establish durability of the foam. Similarly, formulations may purposefully be formulated to more rapidly dissolve when exposed to heat. For example, some bodying agents will dissolve when heated to 32° C—normal body temperature. These thermolabile foams will remain relatively stable at room temperature but begin to melt when they make contact with warm skin.

The density of foams is approximately one-tenth that of traditional vehicles. Easy spreadability of foams is identified as a benefit in treatment of large surface areas and hair-bearing skin, but it is also a benefit for inflamed skin. This is because ease of spreading reduces the need to apply pressure or maintain prolonged contact with the sensitive diseased area.

Additional benefits of foams include lack of stickiness or shininess upon application and, conversely, a tendency to absorb and penetrate quickly. Upon application to hair-bearing skin, the foam vehicle breaks down, allowing the super-saturated secondary formulation to travel down the hair shaft and enter the stratum corneum via the appendageal route. Unlike low viscosity solutions, which can flow away from the application site, foams tend to remain in the area where they are applied.

Patients have demonstrated a preference for and a high level of acceptance of foams. In one study, 20 patients with psoriasis participated in a focus group exploring topical vehicle preferences. The patients sampled different topical psoriasis medications, assessed the effects of the vehicles on quality of life (QOL), and completed a preference measure for each vehicle. The focus group sessions resulted in the development of a seven-item preference measure. Results showed that patients preferred foam and solution vehicles over cream, gel, and ointment vehicles ($p < 0.01$). There was no significant difference between preferences for daytime and nighttime application of vehicles. A subsequent study using the same preference measure found significant patient preference for foams in the management of scalp psoriasis specifically.

It should also be noted that non-prescription foams containing sunscreens, germicides/antibacterials, or keratolytics are available on the market.

**Foam Formulations in Clinical Practice**

The first widely successful topical foam formulations available in the
CHANGING the LANDSCAPE

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INTRODUCING
A Comprehensive, Steroid-Free Regimen for PRURITIC DERMATOSES

NEW!
Atrapro™ ANTIPRURITIC HYDROGEL

NEOSALUS® FOAM • CREAM • LOTION

See reverse for Prescribing Information  Products Prescribed Separately
# ATRAPRO™ Antipruritic Hydrogel

**Rx Only — For Topical Dermatological Use Only**

## DESCRIPTION

ATRAPRO™ Antipruritic Hydrogel is a non-oily, pH neutral hydrogel dressing formulated for the relief of pain, burning and itching associated with various dermatoses, including atopic dermatitis and radiation dermatitis. It helps to relieve dry, itchy skin by maintaining a moist wound and skin environment, which is beneficial to the healing process.

## INDICATIONS FOR USE

Under the supervision of a health care professional, ATRAPRO™ Antipruritic Hydrogel is indicated to manage and relieve the pain, burning and itching experienced with various dermatoses, including atopic and radiation dermatitis.

ATRAPRO™ Antipruritic Hydrogel may be used also to relieve the pain of first and second degree burns. ATRAPRO™ Antipruritic Hydrogel helps to relieve dry, itchy skin by maintaining a moist wound and skin environment, which is beneficial to the healing process.

## CONTRAINDICATIONS

Known hypersensitivity to any of the ATRAPRO™ Antipruritic Hydrogel ingredients.

## PRECAUTIONS

ATRAPRO™ Antipruritic Hydrogel is to be used only as directed by a healthcare practitioner. Do not use in areas which may be contaminated. Avoid contact with the eyes. If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued and the prescribing healthcare practitioner consulted.

## WARNINGS

Do not use if the inner seal is missing or damaged. For topical external use only. Not for injection.

## KEEP THIS AND ALL OTHER MEDICATIONS OUT OF THE REACH OF CHILDREN.

## DIRECTIONS FOR USE

ATRAPRO™ Antipruritic Hydrogel should be applied to affected area three times a day (or as needed). Gently spread over the entire area to create a thin layer. Allow to dry, bandage as needed. Shake well before each use.

## STORAGE

Store in a cool, dry place. Store in its original container. Store at room temperature 15°C to 25°C (59°F to 77°F). Do not use near an open flame or heat sources. Do not freeze.

## HANDLING & DISPOSAL

ATRAPRO™ Antipruritic Hydrogel is non-irritating, non-cytotoxic and non-sensitizing to skin and eyes. Special handling or disposal precautions are not required.

## STABILITY PERFORMANCE TESTING: ATRAPRO™ Dermal Spray with Preservatives has been evaluated by the USP-35-Antimicrobial Effectiveness Test and in time-kill studies for preservative effectiveness.

## Table: Stability Performance Testing

<table>
<thead>
<tr>
<th>Name of Organism</th>
<th>Log Reduction (30 sec.)</th>
<th>Time to Kill</th>
<th>Percent Reduction</th>
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<tbody>
<tr>
<td>Staphylococcus aureus MRSA</td>
<td>6.34</td>
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<tr>
<td>Enterococcus faecalis VRE</td>
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<td>Streptococcus pyogenes</td>
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</table>

## HOW SUPPLIED

ATRAPRO™ Dermal Spray with Preservatives is supplied in an 8 fluid ounce (236 mL) spray bottle bearing the NDC number 23710-365-09.
dermatology marketplace were hydroethanolic foam formulations of corticosteroids. Clobetasol propionate 0.05% foam (Olux, Stiefel/GSK) and betamethasone valerate 0.12% foam (Luxiq, Stiefel/GSK) were introduced in the early 2000s. These are based on the VersaFoam-HF vehicle system. Alcohol within the foam is the primary solvent but also acts as a penetration enhancer, reversibly altering the barrier properties of the stratum corneum, and driving drug across the skin membrane via the intracellular route. This is in contrast to hydration of intercellular spaces in the stratum corneum in order to facilitate drug delivery. 

Data confirm that foam formulations can achieve high concentrations of active corticosteroid in the skin. In fact, one analysis showed that clobetasol 0.05% foam achieved effective levels of skin concentration that were higher than those achieved through oral dosing of prednisone. Of further note, the analysis showed that the only other topical formulations to achieve effective concentrations in the skin higher than those for oral administration were hydrocortisone 2.5% ointment and triamcinolone 0.1% ointment. There is a common perception that, due to their occlusive properties, ointments encourage penetration of corticosteroids. In fact, some clinicians consider an ointment formulation of a given corticosteroid to be of a higher poten-

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**Multi-phase Foams**

**Bi-phasic Foams:**
Solution (solvent, foaming agent, foam stabilizer) + Gas phase (propellant vapor)

**Tri-phasic Foams:**
Lipid phase + Water phase + Gas phase (propellant vapor)

*When the valve is depressed, the propellant vapor pushes fluids down and up through the valve.*
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class than the same molecule in a lotion or cream vehicle.

These ethanolic foam vehicles are thermolabile, dissolving at body temperature to provide good spreadability and cosmetic elegance. As discussed earlier, enhanced drug delivery associated with foams does not depend solely on alcohol content. The natural dissolution of the foam creates a supersaturated drug solution in the propylene glycol-rich secondary formulation that remains on the skin after evaporation of the alcohol and propellants. Supersaturation provides a driving force for drug delivery into the skin.

Due to the alcohol content of hydroethanolic foams, these have been associated with a potential for transient stinging or burning upon application, which may limit their usefulness for some patients. Based on the results of studies demonstrating high patient satisfaction with hydroethanolic foams, however, it is evident that any temporary application site stinging/burning does not hinder treatment for most patients.

Since the introduction of the corticosteroid foams, other formulations based on VersaFoam HF have come to market. Ketoconazole foam 2% (Extina, Stiefel/GSK) is indicated for the management of seborrheic dermatitis. In clinical trials of Extina, a significantly greater percentage of subjects achieved treatment success (IGA of 0 or 1) using ketoconazole foam than vehicle foam (56% and 42%, respectively; \( p < .0001 \)) at week four. In trials, the ketoconazole foam formulation used at various body sites was shown to be equivalent to ketoconazole cream and was well-tolerated with a low incidence of treatment-related adverse events (AEs). AEs were reported in just 14 percent of subjects or 59/427. In treatment or placebo foam vehicle was applied twice daily for four weeks to the face, scalp, or body.

Calcipotriene 0.005% foam (Sorilux, Stiefel/GSK) has also recently been approved by the FDA for treatment of psoriasis. In two multi-center, randomized, double-blind, vehicle-controlled clinical studies, a total of 659 subjects with psoriasis were randomized 2:1 to Sorilux Foam or vehicle. Subjects applied medication twice daily for eight weeks. At Week 8, 14 percent of subjects in one study and 27 percent in another (versus seven percent and 16 percent, respectively, of those receiving vehicle foam) achieved treatment success. In clinical trials, erythema was the only AE reported in more than one percent of subjects and at a higher rate than with placebo foam.

Despite favorable patient reaction to original ethanolic foams and their documented efficacy, a newer foam vehicle has been developed to provide emollient effects. Whereas the original VersaFoam-HF hydroethanolic foam formulation of Olux contains 60 percent ethanol, new Olux-E (clobetasol propionate 0.005%, Stiefel/GSK) based on VersaFoam-EF emollient foam technology does not contain any ethanol. The formulation contains propylene glycol and isopropyl myristate, which are both penetration enhancers. However, it also includes emollient ingredients, such as cetyl alcohol, cyclomethicone, white petrolatum, and light mineral oil. The emollients counter any drying or potentially irritating effects of the penetration enhancers, thereby hydrating the skin and providing a lubricant film to counteract sensations of
stinging, burning, and dryness. The propellant is propane/butane.

In a randomized study of subjects 12 years of age and older with moderate to severe atopic dermatitis, 251 subjects were treated with Olux-E Foam and 126 subjects were treated with vehicle foam twice daily for two weeks. At the end of treatment, 131 of 251 subjects (52 percent) treated with Olux-E Foam achieved treatment success, compared with 18 of 126 subjects (14 percent) treated with vehicle. Treatment success was defined by an Investigator’s Static Global Assessment (ISGA) score of clear (0) or almost clear (1) with at least 2 grades improvement from baseline, and scores of absent or minimal (0 or 1) for erythema and induration/papulation.

In an additional randomized study of subjects 12 years of age and older with mild to moderate plaque-type psoriasis, 253 subjects were treated with Olux-E Foam and 123 subjects were treated with vehicle twice daily for two weeks. At the end of treatment, 41 of 253 subjects (16 percent) receiving active treatment achieved treatment success, compared with five of 123 subjects (four percent) treated with vehicle.

Use of foams is not limited to hair-bearing skin or large surface areas. For example, data confirm the
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The efficacy of Olux-E foam for non-scalp psoriasis. In a trial of 81 individuals with mild to moderate psoriasis, subjects were randomized in a 3:1 ratio to apply clobetasol propionate emollient foam or placebo to treat psoriasis involving nonscalp sites. Response was assessed at weeks 2 (end of treatment) and 4 (follow-up). The investigator's and subject's global assessment of the response at week 2 favored clobetasol propionate emollient foam versus vehicle ($p<0.0005$), and improvement persisted through week 4. No subject withdrew due to adverse events. Twice-daily application was well tolerated, with compliance rates exceeding 90 percent. A recent study demonstrated the efficacy and tolerability of Olux-E foam for the management of hand dermatitis. A minimum 1-grade improvement in the ISGA was achieved by 96.7 percent (29/30) of subjects at day 15, with 80 percent (24/30) of subjects achieving a score of 0 (clear) or 1 (almost clear). Clobetasol propionate 0.05% EF foam appeared to be safe and well-tolerated, with only four subjects experiencing treatment-related adverse events. A recent advancement in foam vehicle delivery is featured in HylatopicPlus Emollient Foam, allowing for the exact same formulation available as HylatopicPlus emollient cream to be administered as a foam. Unlike ethanolic foam formulations, which may be associated with transient burning/stinging or drying, this unique foam formulation offers primarily emollient properties—the same emollient effects as its counterpart cream. The prescribing information for the two delivery systems is the same, with the lone different ingredient between HylatopicPlus Cream and HylatopicPlus Foam being the propellant Hydrofluorocarbon 134a present in the latter. The technology used in HylatopicPlus Foam is Delevo Foam Technology. HylatopicPlus is a prescription-only medical device indicated to manage and relieve the burning, itching, and pain experienced with various types of dermatoses, including atopic dermatitis, allergic contact dermatitis and radiation dermatitis. HylatopicPlus also helps to relieve dry, waxy skin by maintaining a moist wound and skin environment, which is beneficial to the healing process.

As a medical device, HylatopicPlus has no “active” ingredient; its benefits are related to its composition of ceramides, fatty acids, and hyaluronic acid (HA). Hyaluronic acid, perhaps most popular as the basis for the current crop of cosmetic dermal fillers, is a naturally occurring humectant present in various human tissues. The polyanionic polysaccharide consists of N-acetyl-D-glucosamine and beta-glucoronic acid and is present in the intercellular matrix of most vertebrate connective tissues. HA is increasingly used in topical therapies for its humectant effects; it retains up to 1,000-times its volume in water. It is also thought to aid in delivery of agents to the skin, perhaps via these hydrating properties and subsequent opening of the intercellular pathways. Within the formulation of HylatopicPlus, HA may aid in the delivery of ceramides to the epidermis. In a recent study, topical application of HA was confirmed to be associated with improvement in skin hydration and elasticity. Hydrating effects are particularly relevant in management of atopic dermatitis and other dermatoses.
In a tape-stripping study conducted to assess reduction in transepidermal water loss (TEWL) associated with various barrier repair devices, 80 tape-stripped skin sites were evaluated in 10 healthy volunteers. While 20 sites were left untreated as controls, remaining sites were randomized to treatment with Hylatopic Plus Foam, Hylatopic Foam, or EpiCeram (Promius Pharma). TEWL was measured at baseline and two hours after product application. At two hours, HylatopicPlus Foam achieved roughly 160 percent barrier repair relative to control sites, and was the only treatment to show statistical significance in the degree of improvement.23

In vivo assessments using Confocal Raman Spectroscopy confirm the barrier repairing effects of HylatopicPlus. In an open-label, bilateral comparison, two sites of intact skin and two sites of damaged skin (exposed to 1% sodium lauryl sulfate (SLS) for 24 hours to simulate a damaged skin barrier) were identified. One intact site and one SLS-exposed site was randomized to receive HylatopicPlus three times daily, but withheld at least two hours prior to spectroscopy assessments. Remaining untreated sites served as controls. As early as two hours post application, skin treated with HylatopicPlus demonstrated an increase in water and lipid content compared with untreated skin. Improvement continued through to the 48-hour and seven-day timepoints.24

In a double-blind, split body study involving subjects with mild to moderate symmetrical atopic dermatitis involving body surface area greater than or equal to 10 percent on the arms or the legs, subjects were randomized to apply hyaluronic acid-based emollient foam or a reference ceramide-containing emulsion cream to one side of the body with the other test product applied to the opposite side. Twenty subjects were enrolled. While both formulations achieved statistically significant improvement in all clinical signs and symptoms of atopic dermatitis by week 4, only HylatopicPlus Foam achieved statistically significant improvement in overall eczema severity by week 2. Subjects statistically significantly favored the foam in terms of ability to spread, moisturize, ease of use, and lack of odor. Subjects also rated the foam higher than the cream for effectiveness and ability to soothe.25

Another study evaluated the short-term effectiveness and appeal of HylatopicPlus Foam compared to pimecrolimus cream 1% in the treatment of AD.26 Subjects with mild to moderate atopic dermatitis across a wide age range from children (older than two years of age) to older adults applied HylatopicPlus Foam to one side of the body and pimecrolimus cream 1% to the contralateral side. Primary efficacy was measured by IGA. After four weeks of treatment, 82 percent of target lesions treated with the foam formulation were scored "clear" (0) or "almost clear" (1). This is compared to 71 percent of target lesions treated with pimecrolimus being graded as "clear" or "almost clear." There was no statistical difference in the efficacy of the two test treatments. No adverse events associated with use of HylatopicPlus Foam were identified in children or adults during this four-week study.27

Delevo Foam technology is also the basis for BenzEFoam 5.3% (benzoyl peroxide, Onset) and BenzEFoam Ultra 9.8% (benzoyl peroxide, Onset). A corneometry study confirmed the moisturizing ability of BPO emollient foam compared to a generic BPO 5% gel. BPO 5.3% emollient foam...
produced a statistically significant increase in skin moisturization values \( p < 0.05 \) compared to the generic gel, which was associated 
with a decrease in skin hydration.28

In a five-week, open-label, single-center study comparing the anti-
P. acnes effects of benzoyl peroxide 5.3% emollient foam and benzoyl peroxide 8% wash, 20 healthy adult subjects with high 
P. acnes densities on their backs (>10,000 colonies per cm²), but no clinical signs of acne were enrolled. Subjects were treated 
with benzoyl peroxide foam 5.3% under supervision by a technician 
at the study center daily during the first two weeks. After Week 2, 
application of the BPO foam was discontinued for one week to 
allow P. acnes regrowth. Beginning at Week 4, subjects were instructed 
to apply a BPO 8% cleanser (once daily for one week then 
once or twice daily during the next week) to the same area when 
showering. One week of treatment with the BPO 5.3% emollient 
foam yielded a 1.93 log reduction in P. acnes counts and a 2.1 log 
reduction after two weeks. There was no reduction in P. acnes 
counts after treatment with the BPO 8% wash. The lack of P. 
acnes activity associated with the BPO 8% wash was suggested by 
the author to relate to the brief skin contact time with the wash-
off product. Because of the reduced density of follicles and lipids on the trunk, compared to the face, BPO particles in suspension 
in the 8% wash may not have had sufficient time to be deliv-
ered.29

Interestingly, the emollient foam appears to optimize delivery of 
BPO and is effective even with short-contact application. In a sub-
sequent pilot study, six patients colonized with P. acnes on the 
back applied BPO 5.3% emollient foam to the back and rinsed it off 
after five minutes. Each subject was treated under supervision by a 
technician at the study center for five days, followed by two days of 
at-home treatment, followed by one more day of treatment at the 
study center for a total of eight 
days of treatment. At Day 9, the mean reduction in P. acnes was 0.6 
log10 cfu per cm² \( p < 0.05 \). The BPO foam demonstrated a signifi-
cant reduction in P. acnes on the back when it was washed off after 
five minutes of skin contact.30

The newer 9.8% foam formulation also significantly reduced P. 
acnes counts when used as a short contact therapy. A two-week open-
label, single center study of short contact therapy involved 20 
healthy subjects (>18 years old) all confirmed to be colonized with 
P. acnes on their backs (>10,000 colonies per cm²).31 For two weeks, 
each subject applied BPO 9.8% foam to the dry back once daily 
and left it in place for two min-
utes before rinsing if off with 
water and wiping the area with a 
cloth. This protocol was per-
formed under supervision at the 
study center during the week and 
unsupervised at home on the 
weekends.

Mean reduction of P. acnes 
counts on the back was 0.91 log 
per cm² after one week of treat-
ment, and 1.66 log per cm² after 
two weeks of treatment with BPO 
9.8% foam \( p < 0.0001 \)—equivalent 
to a 98.3 percent reduction in P. 
acnes counts. The two-minute con-
tact time is longer than with a 
BPO wash applied to the back and 
rinsed off immediately, as is done conventionally.

Emollient characteristics of the 
foam coupled with short duration 
of contact are expected to mini-
mize BPO irritation while provid-
ing adequate antimicrobial effect. BenzeFoam and BenzEFoam Ultra contain Micronized BPO particles that are smaller than the follicular orifice (~10µm), small enough to penetrate the pilosebaceous unit. Studies demonstrate that the particles remain uniformly dispersed throughout the product with limited formation of large clusters.28

Another emollient foam-based vehicle formulation is NeoSalus from Quinnova, which features the Proderm Technology water-lipid based delivery system. The main components of Proderm Technology (also used in Salvax, Hydro, and Tersi brands) are physiologic lipids palmatic acid and stearic acid. Additionally, it contains the humectant glycerin and emollient dimethicone, as well as fatty acids (stearic acid/palmitic acid) and povidone.

The three primary components of Proderm, then, are protective, reparative, and moisturizing. As such, Proderm is described as a tri-phasic emulsion that, upon application, separates into three distinct layers with variable depths of penetration: primarily on the skin, within the stratum corneum, and into the epidermis. First, dimethicone in NeoSalus forms a protective layer on the skin, creating a physical barrier against penetration of irritants. At the same time, fatty acids penetrate the epidermis where they play an active role in skin barrier restoration and repair. Fluorescent microscopy was used to demonstrate the degree of penetration and the location of fatty acids and dimethicone in NeoSalus relative to petrolatum. Fluorescent labeled fatty acid was added in trace amounts to NeoSalus, while dimethicone and petrolatum are spontaneously fluorescent. Two hours after the formulations were applied to hairless mice, skin samples were taken for fluorescent microscopy. Fluorescence microscopy of normal skin showed minimal fluorescence. Skin treated with petrolatum showed strong fluorescence in the stratum corneum, but no penetration into the viable epidermis, while NeoSalus-treated skin showed dimethicone in the stratum corneum and fatty acid penetration through the stratum corneum and throughout the epidermis. Finally, glycerin and other humectant ingredients attract moisture to the stratum corneum.

The foam formulation is designed to absorb quickly, leaving no residue, and has very good tolerability. In clinical trials of NeoSalus including 161 patients, just four reversible adverse events were reported (2.48 percent), and none were serious. Since the product was introduced in Europe in 1998, there have been only five reports of local intolerance reported. Across studies, about three-quarters of subjects (76.6 percent) reported benefits, improvement in their condition, and satisfaction with the product.

The hydrating effects of the foam formulation have been demonstrated clinically. An unpublished study of electrical capacitance in subjects with atop dermatitis33 showed improvements in hydration in skin treated with NeoSalus compared to control sites. Twenty four subjects with atop dermatitis but with clinically normal-appearing skin were included and completed this randomized study. Subjects underwent a two-week washout period during which they used no emollients. At baseline, TEWL measurements were taken in all subjects. After baseline measurement was taken, subjects with AD applied NeoSalus to an area of 100 cm² on the volar aspect of a randomized forearm twice or three-times daily for two weeks. The untreated contralateral forearm was used as a control. Measurements on days 10 and 21 both indicated an increase in capacitance after treatment and no change in TEWL, i.e. a moisturizing effect without an impairment of skin barrier function. Because of its protectant properties, NeoSalus has demonstrated benefit as a physical barrier for the skin against irritants. In a clinical study to determine the efficacy of NeoSalus in controlling chronic inflammation associated with hand dermatitis, primarily of an occupational nature, 31 subjects with recalcitrant chronic
hand dermatitis of at least 12-month duration who were unresponsive to standard therapy were enrolled. Subjects received NeoSalus with instructions to use at least three times daily, especially while at work. The skin was evaluated by the investigator and by the patient initially and at weeks 2 and 8 for parameters including redness, scaling, fissuring, blistering, and pruritus on a 10-point scale. Use of topical corticosteroids was recorded, and no systemic therapies other than antihistamines were allowed. Six weeks of NeoSalus therapy led to a statistically significant 40 percent mean reduction of hand dermatitis based on IGA score.

Protectant and healing effects of NeoSalus have been suggested in studies of patients with incontinence-induced dermatitis. Adult subjects who used NeoSalus foam, which was well-tolerated in the diaper area, demonstrated improvement in all symptoms of dermatitis and maintained skin integrity through five weeks of maintenance use.

To assess the protectant and anti-inflammatory properties of NeoSalus, a randomized, controlled clinical study was conducted to compare the irritation caused by 10% SLS in skin treated with NeoSalus and untreated controls. A single application of NeoSalus prevented irritation and inflammation associated with SLS exposure in susceptible individuals over a 10 day period. The mean irritancy score was 50 percent lower with NeoSalus pretreatment compared to without it.

A survey of hair stylists using NeoSalus found that a significant proportion (88 percent) indicated that the foam protected their hands from everyday occupational harm. Of those who typically experienced symptoms of dermatitis, 90 percent felt the foam improved symptoms, such as dryness, chapped skin, or pruritus.

Data also indicate that NeoSalus foam may improve wound healing and reduce inflammation. Daily application of NeoSalus to a split thickness skin graft wound in the pig accelerated the rate of wound healing compared to a wound healing ointment and standard of care. Application of NeoSalus was associated with substantial reduction in the size of the wounds over time and a significant decrease in the time to complete closure. Compared to control sites, NeoSalus treatment was associated with reduced incidence of localized erythema, and it decreased the amount of time that exudate was present at the site of injury. Histological examination...
Possible Benefits of Foam Formulations

- Comparable cost to other formulation types.
- Ease of application to hair-bearing and other skin.
- Easy to spread; Reduces need to manipulate inflamed skin.
- High level of patient satisfaction.
- May incorporate barrier repairing and/or emollient ingredients.

revealed reduced subacute and granulomatous inflammation and enhanced neovascularization in wounds treated with NeoSalus.

An Evolving Delivery Form

Topical foam vehicle delivery systems are relatively new to dermatology, yet they already have established an important role in patient care. While foam vehicles have already undergone several formulation enhancements, additional advancements are anticipated. Next generation emollient foams are especially useful for inflammatory skin conditions associated with an impaired epidermal barrier.

Despite the relatively higher costs associated with the development and manufacture of these specialized formulations, data suggest that foams may not in actual use cost more than other formulation types. The high level of patient satisfaction and ease of application associated with topical foams will likely drive continued development in both the prescription and non-prescription skin care realms.

17. Sorilux P.
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27. Data on file, Onset Dermatologics
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When we set out to create innovative skin products, we talked with dermatologists and consumers to help gain valuable insight. We understand that patients care about their skin and its appearance, that’s why we’re committed to keeping skin healthy. The result is great products that we believe are redefining the world of dermatology.