Research Article

A Recalcitrant Skin Fissure Treated with an Anionic Polar Phospholipid Emulsion

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Abstract

Purpose: Recalcitrant fissures located on weight-bearing skin surfaces are often challenging to heal. This study compares the efficacy of an Anionic Polar Phospholipid (APP)-based skin cream emulsion to a standard moisturizing cream treatment regimen in a patient with a foot fissure unresponsive to conventional treatment.

Methods: Treatment included a twice daily topical application to the cutaneous surface of the foot fissure as well as the perifissure area with an APP-skin cream (test product) for 3 wks. The APP-skin cream was comprised of phospholipids including phosphatidylglycerol, phosphatidylinositol, and phosphatidylserine, in an aqueous emulsion of hydrogenated vegetable oil. Skin cream treatment was then discontinued for a wash-out period of 4 wk. Treatment was then reinstated twice daily using a standard reference moisturizing cream for 3 weeks. Subjective and objective dermatologic findings were recorded at baseline and weekly throughout the 10-week period.

Results: There were marked subjective and objective improvements in the fissure using the test product following the initial 3-week treatment. After the subject had discontinued the test treatment for 4 weeks, the fissure resembled its nascent pretreatment appearance and baseline symptoms reoccurred. The treatment regimen was reinstituted using the reference moisturizer for a 3-week course. In contrast to the marked improvement in signs and symptoms with the test product, there was only mild to moderate improvement using the reference moisturizing cream.

Conclusions: This case demonstrates the superior resolution of a painful skin fissure using an oil-in-water-based skin cream supplemented with APP compared to a skin cream reference common moisturizer. Topical treatment of a recalcitrant skin fissure using APP in an oil-in-water emulsion skin cream is a novel application for this phospholipid technology.

Keywords: Anionic polar phospholipids; APP; Foot; Phosphatidylglycerol; Phosphatidylinositol; Phosphatidylserine; Skin; Skin cream; Skin fissures

Introduction

Difficulty healing fissured skin is pronounced in regions where traction movement of the skin is unavoidable. These regions, when associated with weight bearing and continual movement of the skin, challenge the elasticity of the skin and may result in fissures. Although these skin fissures are commonly treated with antibiotic containing petrolatum-based emollients, petrolatum only serves as a skin occlusive, may have no healing properties, and may increase inflammation with slowed healing.

Healing of these fissures may occur more rapidly when a humectant is topically applied to the skin. There are several humectants found in soaps, cosmetics, and moisturizers.
They include glycerin, honey, aloe Vera, and lactic acid. An alternative is an Anionic Polar Phospholipid (APP)-hydrogenated vegetable oil-based emulsion, containing phosphatidylserine, phosphatidylinositol, and phosphatidylglycerol. When this emulsion is applied topically, the hydration status of the skin surface is improved with repair of the bricks and mortar of skin [1-3]. This APP technology fortifies and stabilizes the lipid layers [4-7].

Eye drops containing APP technology when topically applied to the ocular surface in patients with dry eye conditions is highly effective [4-7]. With instillation of eye drops into the tear film onto the ocular surface, spillage onto surrounding periorbital skin often occurs especially at the lateral canthus. Clinical observation of periorbital skin abnormalities such as the static fine lines and wrinkles found at the lateral canthus or “crows feet”, demonstrated improvement. This observation was thought to be due to the humectant property of the anionic phospholipid formulation. Accordingly, the APP-based emulsion used as an eye drop was reformulated into a skin cream emulsion in a humectant. Using this emulsion, skin conditions including seborrhea [8,9], psoriasis [8,9], and radiation burns [10], were treated. APP-based emulsion was observed to improve dry skin even on the calloused rim of the heel of the foot [8]. This observation suggested that the APP emulsion skin cream may be effective in healing a fissure on the hyperkeratotic foot skin.

There are a number of factors that can impede healing of a fissure such as (1) skin with an increased degree of keratinization, (2) skin with reduced degrees of moisturization, and (3) skin in locations where repetitive movement is necessitated and subjected to physical pressure, such as weight-bearing of the ventral surface of the foot. Traditional humectants and moisturizers may be ineffective under these conditions.

The skin region overlying the distal portion of the first metatarsal of the foot represents challenges due to the increased stress of the skin, which occurs during the activities of standing, walking, or running. This is especially important in people with a high Body Mass Index (BMI). Skin fissures located on the ventral plantar surface of the foot, and more specifically the rounded protuberance over the distal portion of the first metatarsal bone of the foot at the base of the big toe, can result in discomfort or sharp pain, which can limit weight-bearing activities. The purpose of this study was to compare the efficacy of an APP-based skin cream emulsion to a standard moisturizing cream treatment regimen in a patient with a foot fissure unresponsive to conventional treatment.

Methods

The patient was a 65-year-old Caucasian male 1.73 m in height weighing 140 kg with a recalcitrant skin fissure located on the ventral skin surface of the left foot. The skin involved in the fissure corresponded to the region over the distal end of the first metatarsal. Informed consent was obtained. All tenets of the Declaration of Helsinki for the protection of human subjects in medical research were strictly observed. Patient history included no smoking of tobacco, occasional use of alcohol, and no diabetes, hypertension, or other diseases affecting the circulatory system. The only pertinent dermatologic history included the occurrence of warty excrescences and psoriasis though not present on the foot. Systemic history otherwise appeared to be non-contributory. The patient denied having any drug allergies. Systemic medication included long-term warfarin sodium prescribed after the patient suffered from an infection of unknown etiology requiring surgical intervention of the right knee unrelated to a vascular diagnosis.

For more than an 11-year period, the patient experienced a poor or absent response to a large (>20) variety of topically applied foot skin preparations (moisturizers and humectants) prescribed in order to heal the fissure. These skin preparations included Over The Counter (OTC) medicated and unmedicated topical creams, lotions, and ointments. These skin care products were used according to manufacturer’s directions, all in an attempt to heal the foot fissure. The severity of the fissure waxed and waned to a mild degree with a number of these skin care products. No or little measurable visual or tactiley appreciated recovery of signs or symptoms occurred.

Examination of the left foot revealed the presence of a deep linear gaping fissure oriented in the sagittal plane and located in the central region of the ball of the foot (Figure 1). The fissure was surrounded by hyperkeratotic, thick, dry, flaky, calloused skin. The base of the fissure had no evidence of hemorrhage or scab. The fissure caused constant moderate to severe discomfort while ambulating such that the patient favored weight bearing on the right foot. Discomfort and difficulty in healing was believed to be further exacerbated with the high BMI.
Figure 1: a) Clinical photograph of foot at baseline prior to treatment demonstrating the dimensions of a recalcitrant foot fissure; b) 1 week following daily treatment using the APP-skin cream; c) 2 weeks following daily treatment using APP-skin cream; d) 3 weeks of following daily treatment using APP-skin cream indicating a closed fissure. All figures approximate the same magnification.

Skin Cream Preparation

Test product

Proprietary APP skin cream: The active ingredients are the anionic polar phospholipids, principally phosphatidylserine, phosphatidylinositol, and phosphatidylglycerol and hydrogenated vegetable oil. These ingredients were prepared in a water-soluble cream formulation. All components comprising the test product (cream) used in this study were Generally Recognized As Safe (GRAS) by the United States Food and Drug Administration (FDA) which are chemicals or substances exempted from the usual Federal Food, Drug, and Cosmetic Act (FFDCA) tolerance requirements.

Comparative reference moisturizer cream: Eucerin® Intensive Repair Extra-Enriched Foot Cream (Beiersdorf AG, Hamburg, Germany). The ingredients listed for this cream are water, glycerin, urea, cetearyl alcohol, sodium lactate, capric/caprylic stearic triglyceride, petrolatum, ethylhexyl cocoate, hydrogenated cocoglycerides, octyldodecanol, aluminum starch octenylsuccinate, dimethicone, sorbitan stearate, PEG-40 castor oil, sodium cetearyl sulfate, carbomer, lactic acid, phenoxyethanol [11]. The Eucerin reference moisturizer was selected as an available OTC and representative of a market leader in the United States at the time of this study.

Treatment Protocol

The patient applied no foot skin preparations for two weeks prior to the initiation of the test sequence. Furthermore, the patient abstained from attempting to perform any self-debridement of loose dry or peeling skin for the same period prior to testing. Other than the test APP cream and the reference moisturizer cream, no other foot products were used during the 10 week course of the test sequence. The foot was cleaned daily in the usual manner by bathing with the same moisturizing soap and warm water regimen customarily used. During the test sequence the patient wore shoes and socks during the course of the day for approximately 12 hours. The brand and make of both properly fit footwear and stockings were not varied during the test sequence. Open label APP skin cream bottles of the same lot number were provided to the patient with specific instructions for application. Creams were applied topically and liberally with the index finger twice daily to the fissure and peri-fissure area. The peri-fissure area included the skin extending no more than 2 cm from any fissure border. The APP-skin cream was repeatedly and successively applied and rubbed into the skin until the skin being treated was unable
to absorb additional cream. This method required 3-5 applications over several minutes of a finger-tip amount before the skin was observed to prohibit further absorption. For the control reference moisturizer cream, the method of application was identical in methodology and amounts used as detailed above for the APP-skin cream.

Test Sequence: After 3 weeks of twice-daily application of the test APP-skin cream, treatment was discontinued for a period of 4 weeks. Subsequently, treatment resumed with the control topicaly applied reference moisturizer. This cream was used and applied in the same manner and frequency as the test cream for a period of 3 weeks. Both the APP and the reference moisturizer creams were fragrance-free.

Data Acquired

Subjective impressions were recorded weekly based on the patient’s grading observations of the degree of peeling, dryness, softness, and smoothness, and any degree of overall improvement of the skin fissure and the hyperkeratosis of the peri-fissure area over baseline. These subjective impressions were considered reliable since the patient had 11 years of treatment experience and was able to articulate the degree of its severity with confidence.

<table>
<thead>
<tr>
<th>Skin Condition</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peeling</td>
<td>No peeling</td>
<td>Mild peeling</td>
<td>Moderate peeling</td>
<td>Severe peeling</td>
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<tr>
<td>Dryness</td>
<td>No dryness</td>
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<td>Moderate dryness</td>
<td>Severe dryness</td>
</tr>
<tr>
<td>Softness</td>
<td>Very soft</td>
<td>Moderately soft</td>
<td>Somewhat soft</td>
<td>Not soft</td>
</tr>
<tr>
<td>Smoothness</td>
<td>Very smooth</td>
<td>Moderately smooth</td>
<td>Somewhat smooth</td>
<td>Not smooth</td>
</tr>
</tbody>
</table>

Table 1: Skin fissure and peri-fissure grading scale for peeling, dryness, softness, and smoothness.

Physical examination of the patient’s foot fissure and peri-fissure area was performed weekly. In addition to patient assessments, dermatologic observations recorded by two independent examiners included visual and palpatory examination for peeling and dryness as well as tactile examination and palpation for softness and smoothness graded on a scale of 0-3. Grading was recorded according to the same scale (Table 1) used by the patient. Grades in 0.5 increments in all categories measured were allowed. All measurements and assessments from both examiners were averaged and disputed differences were few and never greater than 0.5. Fissure size was measured with a millimeter ruler and fissure depth estimated. Photo-macrography was used to document the baseline condition of the fissure prior to starting treatment and thereafter prior to examination and on a weekly basis throughout the 10-week period. The overall assessment of improvement or no improvement in the condition of the fissure and peri-fissure area was made on a composite of visual observation, physical measurements, and palpatory examination scores.

Results

At baseline, fissure length was 21.0 mm, width 1.5 mm, and depth was more than 1 mm (Figure 1a). Examiner objective assessment (Table 2) revealed the skin of the fissure and peri-fissure areas were observed to have severe peeling (Grade 3.0), severe dryness (Grade 3.0), and absence of softness (Grade 3.0) and smoothness (Grade 3.0). Subjective assessments of the fissure and peri-fissure area by the patient indicated severe peeling (Grade 3.0), severe dryness (Grade 3.0), and no evidence of softness (Grade 3.0) or smoothness the surface being rough (Grade 3.0).
After 1 week of topical application of the test cream (Figure 1b), fissure dimensions changed minimally from baseline. With objective examiner evaluation peeling was improved (Grade 1.0) and dryness was moderate (Grade 2.0). Softness and smoothness improved to somewhat soft and somewhat smooth to Grade 2.0. The overall status of the fissure appeared to have improved considerably in physical appearance and palpatory examination. Subjective patient assessments by degree of peeling improved to Grade 1.5, dryness to moderate (Grade 2.0) and softness and smoothness to somewhat soft and somewhat smooth (Grade 2.0). The subjective patient impression of overall improvement was estimated at 50%.

After 2 weeks of using the test cream (Figure 1c), fissure length decreased to 17 mm, width 1 mm, and depth appeared the same. Objectively, peeling had decreased to Grade 0.5 and dryness had decreased to mild (Grade 1.0). Softness and smoothness were Grade 1.5. Subjectively the patient graded the peeling and dryness as Grade 0.5, softness as Grade 1.5, and smoothness as Grade 1.0. The overall subjective improvement was estimated at 75% improvement over baseline.

After 3 weeks (Figure 1d), fissure dimensions were unchanged from the 2-week time point. Peeling was absent (Grade 0) and dryness was absent (Grade 0). Softness had further improved to Grade 1.0 from week 2, and smoothness remained the same as week 2 (Grade 1.0). Subjectively the patient graded the peeling as 0 and dryness as Grade 0, softness was Grade 1.0, and smoothness was Grade 0.5. The overall subjective improvement was reported to be 80% over baseline. The treatment with the test cream was promptly discontinued after 21 days and no skin cream was applied during the 4-week washout period.

After 7 weeks, 4 weeks after discontinuing the test cream (Figure 2a), treatment with the reference moisturizer was begun. At that time, the fissure measured 16 mm in length, 1 mm in width and appeared no greater than 1 mm in depth. Peeling and dryness appeared to have returned to baseline severe (Grade 3.0) resembling the original baseline 7 weeks earlier. Softness and smoothness were Grade 3.0. Subjectively the patient graded peeling as Grade 3.0, dryness as severe (Grade 3.0), and softness and smoothness were each Grade 3.0. The patient’s subjective impression of the signs and symptoms of the fissure compared to the original baseline was minimal and unmeasurable; however, the patient commented that the fissure still was improved over the original pretreatment baseline. At 7 weeks, the patient was unable to assign a percentage improvement over the original baseline at 0 weeks.

After week 8 (Figure 2b), fissure dimensions while continuing treatment with reference moisturizer remained unchanged from week 7. Peeling was moderate (Grade 2.5). Dryness was severe (Grade 3.0). Softness and smoothness were Grade 2.5. Subjectively the patient graded peeling as Grade 2.0 and dryness as Grade 3.0. Softness and smoothness were unchanged (Grade 3.0) from week 7. Improvement in signs from the 7-week time point (pre-reference moisturizer baseline) was minimal and improvement of symptoms was ≤25%.

After week 9 (Figure 2c), the fissure length was 15 mm, width 1 mm, and depth appeared less. Peeling was mild (Grade 1.5), and dryness improved to moderate (Grade 2.0). Softness was graded as somewhat soft (Grade 2.0). Smoothness was graded as somewhat smooth (Grade 2.0). Subjectively the fissure remained mildly improved, and the patient graded peeling as Grade 1.0 and...
dryness as Grade 2.0. Softness and smoothness were graded as somewhat soft and somewhat smooth respectively (Grade 2.0), and overall was estimated to be 50% improved over pre-reference moisturizer use beginning at the 7-week time point.

After week 10 (Figure 2d) fissure dimensions remained the same as at 4 weeks. Peeling was grade 0.5, and dryness was Grade 2.0. Softness and smoothness remained the same as at week 9. Subjectively the patient graded peeling as Grade 0.5 and dryness as Grade 1.5. Softness and smoothness had improved to Grade 1.5. Overall improvement was estimated as 50% over pre-reference moisturizer use beginning at 7-weeks.

![Figure 2](image-url)

**Figure 2:** a) Clinical photograph of foot fissure after cessation of all treatment for 4 weeks; b) 1 week following daily treatment using the reference moisturizer; c) 2 weeks after daily treatment using the reference moisturizer foot cream; d) 3 weeks of daily treatment using the reference moisturizer. All figures approximate the same magnification.

**Discussion**

Foot fissures originating in weight-bearing regions are common, can be difficult to heal, and can be painful enough to make ambulation difficult. Fissures of the foot may be severe enough to preclude ambulation. Left untreated eventually fissures can lead to a portal of entry of infection with possible complications. This report demonstrates the superiority of an Anionic Phospholipid (APP)-based cream over a reference moisturizer in a patient with a recalcitrant foot fissure. The improvement, superiority and maintenance of the skin with APP emulsion has been demonstrated in other skin maladies involving deficient skin hydration [8,9].

Healing a fissure resulting from poorly hydrated skin and especially on skin with hyperkeratinized epithelia such as the sole of the foot requires hydration [12,13]. Hydration of dry surface cells and intercellular “bricks and mortar” [2,3] leads to softening of the skin providing the medicant is massaged into and taken up by the skin cells and surrounding intercellular lamellae. Even without debridement of epithelium in the present case, the skin softened with daily massage with skin cream containing APP. It is hypothesized that the APP penetrates the skin and forms “chemical complexes,” i.e., bonds in the cell membrane lamellar bilayers [8,9].

The skin fissure was present on the ball of the foot overlying the distal region of the first metatarsal bone, that region between the toes and the arch of the foot or the region that bears the greatest weight when weight is redistributed anteriorly in the heel to toe movement during ambulation. In the present case, the fissure was present for over 11 years and numerous attempts to heal the fissure with a variety of lubricants and medicaments were not successful. With the ball of the foot having the greatest weight, the skin fissure was difficult to heal as the supported weight would stretch the skin resulting in structural deformation that discouraged healing. The
fissure in this case was oriented perpendicular to the toes and not aligned with foot skin rhytids (Figure 1). With ambulation and accompanying flexion of the foot, one might expect a fissure as well as rhytids to align parallel to the base of the toe’s perpendicular to the major axis of the foot. Since a rhytid may be the forerunner of a fissure, the perpendicular alignment of the fissure in this case is unexpected. As such, with natural to-and-fro foot movement, e.g., during standing (balancing), walking, or running, might discourage healing.

Moisturizing skin creams available commercially primarily are used to maintain the stratum corneum. These creams, however, address symptoms [e.g., dryness, peeling (desquamation)] but not the primary cause of most skin maladies, which are the compromised bilayers and lamellae of the lamellar system [8,9]. The lamellar system is present in the extracellular spaces between the corneocytes, which are filled with polar lipids that form the bilayers and lamellae (Figure 3). In a well-functioning lamellar system, each lipid bilayer is separated from adjacent lipid bilayers by a layer of organized water. These lamellae are stacked and fill the spaces between the corneocytes. If the lipids are compromised or water evaporates, a variety of skin maladies can result including dryness, peeling (desquamation) and the appearance of rhytids of the skin. Organization of the lamellae is a biochemical process, and, as such, lamellae can repair themselves without intervention by living cells provided the requisite polar molecules are present. Desiccation occurring in the lamellar system can cause the bilayers to align themselves into a crystalline-like structure. Such an arrangement compromises the plasticizer (flexibility) property of the interstitial lamellar layers, causing the skin to become hard, brittle, and eventually fracture and form a fissure [14]. When skin is treated with APP cream and the bilayer lamellar system repaired, the natural hydration and organization of water is believed to be restored [15]. The delivery of APP cream into the skin is supported by permeation studies [16].

Figure 3: (Top Figure) Oil (yellow figure) and water (blue figure) with natural opposition to one another (arrows). (Middle Figure) A schematic representation of an assemblage of Anionic Polar Phospholipid (APP) molecules (red) with hydrophobic (oil seeking tails oriented on top) and hydrophilic (water seeking polar head groups oriented on bottom). (Bottom Figure) An assemblage of APP molecules interacting strongly with hydrocarbon oily tails (junction between red and yellow figures) and with polar head groups interacting strongly with water (junction between red and blue figures), the complex acting like a zipper.
There are two potential mechanisms of action unique to the APP cream [8,9]. The first is the repair of the lamellar system via penetration of APP and triglycerides into the bilayers of the stratum corneum. The second is the organization of water through the charged nature of the anionic polar phospholipids (phosphatidylglycerol, phosphatidylinositol, phosphatidylserine) involved. Such actions are thought to repair defects or holes in the strata that result from skin damage and resultant loss of natural polar lipid components. The repair of defects in the lamellar system is due to both the APP and the triglyceride components of the skin cream [8,9]. These molecules are polar and water seeking [3]. Thus, they are attracted to the water in the stratum corneum. Additionally, other layers of the epidermis and underlying dermis are all dependent on how severely the more superficial skin layers have been damaged. This is significant in the case of a skin fissure which affects multiple layers of the skin. The penetrating ability of the APP-skin cream [17] results from the thermodynamics of anionic polar phospholipids. As a result of thermodynamic properties, the phospholipids (phosphatidylglycerol, phosphatidylinositol, phosphatidylserine) contained in the APP formulation provide the driving force for this penetrating action. This includes amphiphilic interactions, such as, hydrogen bonding and organization of water, electrostatic interactions, and the hydrophobic interaction among the lipid side chain phospholipid residues. The hydrophobic interaction is the process that results in water organization (Figure 3) [18].

An APP molecule penetrating the stratum corneum upon arriving at the defective lipid bilayer, will insert itself beside other polar lipids in the existing bilayer. The APP molecule becomes oriented via local physicochemical forces. These forces orient phospholipid hydrophilic ends to hydrophilic ends and hydrophobic ends to hydrophobic ends (Figure 4). Akin to a zipper closing [1,3], the insertion of APP molecules can fill the lamellar system defect, sealing a gap. Sealing a gap re-establishes the organization of the water layers between the lamellae. This organization of the water layers re-establishes hydration of the skin tissue.

Analogous to dry skin, the treatment of dry eye using a novel Anionic-Polar-Phospholipid-(APP)-based emulsion, has been shown to be more effective than any other artificial tear to date, its duration time on the ocular surface has been demonstrated to be >24-hours [4,5]. Although the duration of action time with the APP emulsion skin cream is not known, we hypothesize that it would be at least equivalent to the duration of the artificial tear preparation [7]. It is expected that the APP emulsion eye drop might have a significantly shorter duration of action due to the fluidity of the tear film. The APP emulsion skin cream, with its rather profound and efficient effect on healing the skin surface, may bear similarities to the eye-drop preparations. In the tear film, the APP emulsion appears to augment and improve the tear film phospholipids that function in joining the superficial hydrocarbon-like lipid layer of the tear film with its underlying aqueous layer [4-6].

For the skin, the APP emulsion skin cream augments the phospholipids in the lamellar system [8,9]. It is of particular interest that the relatively thick keratinized stratified squamous epithelium of the skin on the ventral surface of the foot permitted absorption of the APP skin cream. This is likely because of the sparse or near absence of the important “mortar” between the cells in such a “hard” skin surface as in the ventral foot. It is the absence, or near absence, of this mortar that likely facilitates the APP skin cream penetration while it fills gaps and rebuilds the tissue, re-establishing skin suppleness and with hydration, skin suppleness as observed in this case.

The principal difference between the APP skin cream and the reference moisturizer was believed to be that APP repaired the fissure faster and more completely over the 3-week course of treatment (Figures 1d and 2d). There was not as dramatic a change in the fissure with the reference foot cream, as the reference cream did not appear to be as effective in closure or repair of the fissure (Figure 2). The ability of the skin to absorb the APP skin cream [16,17] and its coincident efficiency of healing was remarkable and well tolerated. Further was the observation that there was no remaining residue from the cream after application by rubbing. The APP cream is not visible and absorbs into the skin [16,17], thus avoiding product soiling of bedding (sheets) or foot coverings nor does it necessitate removal of residual product from the skin. Removal of product is not necessary due to its ability to absorb into the skin. As a result the APP skin cream is more effective, saves application time, and appears to obtain superior results. Traditionally moisturizers and humectants frequently require removal of unwanted residues. The presence of residues affects quality of life, ease of use, and soiling of clothing by attracting foreign bodies on residual skin cream product. The APP-skin cream resulted in marked improvement after 1 week (Figure 1b) compared to the reference moisturizer (Figure 2b) considered to be a market leader. APP cream continued to show observable improvement throughout the 3-week test period (Figures 1c and 1d).
**Figure 4:** Illustrated model after Rawlings [20] of the covalently bound lipid bilayers (medium sized round circles) separated by water layers in the *stratum corneum* (main figure). The hydrophilic polar headgroups (small round solid red circles) face and organize the water (blue) into layers. The inset, detailing the Lipid Bilayers (upper right) is depicted by a small white square in the main figure. The hydrophobic lipid tails of polar phospholipids are oriented in such a fashion so as to organize the phospholipids into a bilayer. Desmosomes are pictured joining skin corneocytes together.

**Conclusion**

In conclusion, these observations demonstrate that the use of APP cream technology may overall improve signs and symptoms of fissures and peri-fissure xerosis of the foot. The importance of being able to improve recalcitrant and painful foot fissures is that it positively affects the quality of life and reduces or prevents the ultimate complications of such fissures. The application of APP cream technology [19] to improve multiple skin conditions or abnormalities is probable. Similar applications to ophthalmic conditions including e.g. dry eye, have demonstrated the healing ability of APP to resolve xerotic disorders of the ocular surface [4-7]. This unique APP technology [19] offers a potential breakthrough in skin repair and wound healing that would reasonably be expected to be applicable to the treatment of a myriad of skin conditions.

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**References**


