Bathing in a magnesium-rich Dead Sea salt solution improves skin barrier function, enhances skin hydration, and reduces inflammation in atopic dry skin

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Abstract

Magnesium salts, the prevalent minerals in Dead Sea water, are known to exhibit favorable effects in inflammatory diseases. We examined the efficacy of bathing atopic subjects in a salt rich in magnesium chloride from deep layers of the Dead Sea (Mavena® Dermaline Mg^{46} Dead Sea salt, Mavena AG, Belp, Switzerland).

Volunteers with atopic dry skin submerged one forearm for 15 min in a bath solution containing 5% Dead Sea salt. The second arm was submerged in tap water as control. Before the study and at weeks 1–6, transepidermal water loss (TEWL), skin hydration, skin roughness, and skin redness were determined.

We found one subgroup with a normal and one subgroup with an elevated TEWL before the study. Bathing in the Dead Sea salt solution significantly improved skin barrier function compared with the tap water-treated control forearm in the subgroup with elevated basal TEWL. Skin hydration was enhanced on the forearm treated with the Dead Sea salt in each group, which means the treatment moisturized the skin. Skin roughness and redness of the skin as a marker for inflammation were significantly reduced after bathing in the salt solution. This demonstrates that bathing in the salt solution was well tolerated, improved skin barrier function, enhanced stratum corneum hydration, and reduced skin roughness and inflammation.

We suggest that the favorable effects of bathing in the Dead Sea salt solution are most likely related to the high magnesium content. Magnesium salts are known to bind water, influence epidermal proliferation and differentiation, and enhance permeability barrier repair.

Introduction

Bathing in the Dead Sea as treatment of skin diseases has been known for hundreds of years.[1] The Dead Sea has an average salinity of 280 g/kg compared with the ocean's average 35 g/kg. It is rich in magnesium, calcium, potassium, and bromine and is depleted in sodium, sulfate, and carbonate ions. The actual salt content depends on the regional location (water is flowing in by the River Jordan), the water depth, and various additional factors.[2] Magnesium salts are quantitatively most important in Dead Sea water. Salt from the Dead Sea is sold in many countries. Mavena® Dermaline Mg^{46} Dead Sea salt (Mavena AG, Belp, Switzerland) is obtained from the depths of the Dead Sea, which is naturally rich in magnesium chloride at a level of 46% in the crystalline form. It also contains 2.2% $CaCl_2$, 0.5% KCl, 0.8% NaCl, small amounts of bromides and sulfates, and water of crystallization.

Biochemical effects of Dead Sea salt therapy have been evidenced *in vitro* and *in vivo*. *In vitro* studies have shown that magnesium bromide and magnesium chloride inhibits the well-known excessive proliferation of psoriatic keratinocytes.[3] Increased levels of magnesium and calcium ions, which may play a role in cell proliferation and differentiation, have been described in psoriatic keratinocytes and after sodium laurylsulfate-induced irritation.[4,5] Early in the process of wound healing the concentration of magnesium ions in wound fluid from porcine and rat skin is elevated.[6–8] Hairless rats fed a low magnesium diet developed a raised patchy erythematous rash consisting of nonfollicular plaques and papules.[9] Magnesium regulates adhesion molecules E-catherin and $\alpha_2\alpha_1$-integrin-mediated migration of keratinocytes.[10] Also, magnesium ions exhibit anti-inflammatory properties; a magnesium ion-containing ointment significantly inhibited the croton-oil-induced inflammation of the skin.[11] Furthermore, beneficial effects of magnesium ions applied locally to the skin of patients with contact dermatitis have been reported by Greiner and Dietzel.[12] Magnesium ions inhibit the antigen-presenting capacity of Langerhans' cells, most

important for sensitization and elicitation of allergic reactions; contributing to the efficacy of Dead Sea salt in the treatment of inflammatory skin diseases.[13]

At the Dead Sea, bathing in the salt water is usually combined with ultraviolet (UV) irradiation.[14] Although such a combination is effective, the benefit of the bathing aspect is emphasized by Even-Paz *et al*. These authors found improvement in psoriasis patients who only bathed in Dead Sea water.[2] In the present study we examined the effect of bathing in a Dead Sea salt solution especially rich in magnesium ions on biophysical characteristics in atopic dry skin.

Materials and Methods

Subjects

The study was approved by the local Ethics Committee. Thirty subjects with known atopic dermatitis (18 males and 12 females, age 20–54 years) according to the criteria of Hanifin and Rajka[15] participated in the study. The subjects did not show an active disease, but exhibited atopic dry skin (xerosis) on the forearms. Subjects were instructed not to use any kind of emollient on the forearms within a 3-day run-in period and during the study. Immunomodulators, in particular corticosteroids, were not allowed within a 3-week run-in period and during the study. The study was performed during winter time in Bonn (Germany) and therefore biologically relevant sun exposure did not occur. Artificial UV-irradiation was also forbidden within a 3-week run-in period and during the study. Subjects submerged their forearm for 15 min in a bath solution containing 5% salt of the Dead Sea (Mavena® Dermaline Mg[46] Dead Sea salt). The control forearm was submerged in tap water only. The temperatures of the bath solutions were 38–42 °C. Bathing was performed daily for 6 weeks. The study was randomized and double blinded. The solutions were prepared by different assistants in different rooms, so the investigators and the volunteers were unaware which receptacle was filled with salt solution and which was filled with water. The Mavena® Dermaline Mg[46] Dead Sea salt contains salt from the depths of the Dead Sea with a high magnesium content of approximately 120 g/kg. Immediately before the study, preceding bathing at baseline (week 0), and 4 h after bathing at weeks 1, 3, 5, and 6, TEWL, skin hydration, skin roughness and skin redness were determined on the volar side of the forearms.

Measurements were carried out at a temperature of 20 ± 1 °C and a relative humidity of 50 ± 10%. Subjects were accustomed to ambient conditions for 30 min before any measurement.

Biophysical measurements

Measurements of transepidermal water loss (TEWL) as a marker of permeability barrier function were performed with the Tewameter TM 210 (Courage + Khazaka GmbH, Cologne, Germany). Measurements were carried out in accordance with the guidelines of the Standardization Group of the European Contact Dermatitis Society.[16] Each value was the average of three measurements.

For the measurements of stratum corneum hydration the Corneometer CM 825 PC (Courage + Khazaka, Cologne, Germany), which registers the electrical capacity of the skin surface, was used. The capacity was expressed digitally in arbitrary units.[17] Three measurements were performed on each test area and the mean was used to define the hydration state of the stratum corneum.

Determinations of skin roughness were performed with the PRIMOS optical 3D *in vivo* skin measurement device (Phase-Shifting Rabbit In Vivo Measurement of Skin; GF Messtechnik, Berlin, Germany). This system allows fast, three-dimensional *in vivo* measurement of the microtopography of the human skin in a noncontact method based on the technology of active-imaged triangulation (three different measurement methods were used). The parameter Rz was calculated by using a phase-shift technique.[18]

Measurements of skin redness were performed with a Chromameter CR 300 (Minolta, Japan). The measurements were taken exclusively in the L*a*b* colorimetry system (L* represents the brightness, a* and b* the hue and color saturation): a* shows the position on the red-green axes and b* on the yellow-blue axes. Increasing redness is shown by an increase of the a* value. Measurements were performed according to the guidelines of the European Society of Contact Dermatitis.[19]

Statistical analysis

Measuring data were computerized using the software Stat graphics for Windows 5.0 (Magnustics Inc, Rockville, MD, USA). Data were statistically analyzed and tested by Wilcoxon's matched-pairs signed-rank test. The 0.05 levels were selected as the point of minimal acceptance of statistical significance.[20]

Results

Transepidermal water loss

We first determined transepidermal water loss (TEWL) as a marker of barrier function before and after 1, 3, 5, and 6 weeks of treatment. Regarding basal TEWL before any treatment revealed two groups, we found 12 volunteers with normal TEWL (< 10 g/hm² subgroup nTEWL) and 18 volunteers with elevated TEWL (> 10 g/hm² subgroup eTEWL). Also, in the literature, normal as well as elevated TEWL in dry skin has been reported.[21–24] Therefore, we performed a subanalysis for all our studies.

In the entire group, there was a slow but constant decrease in transepidermal water loss after treatments with the Dead Sea salt solution. In contrast, TEWL was not reduced after bathing in tap water. A comparison between the salt solution and tap water treated forearm revealed a significant decrease in TEWL after 5 and 6 weeks of treatment (after 6 weeks: −19%, $P < 0.05$) (Fig. 1a–c). In the subgroup eTEWL of subjects, which showed elevated TEWL (> 10 g/hm²) before the study, a significant decrease compared with the controls was

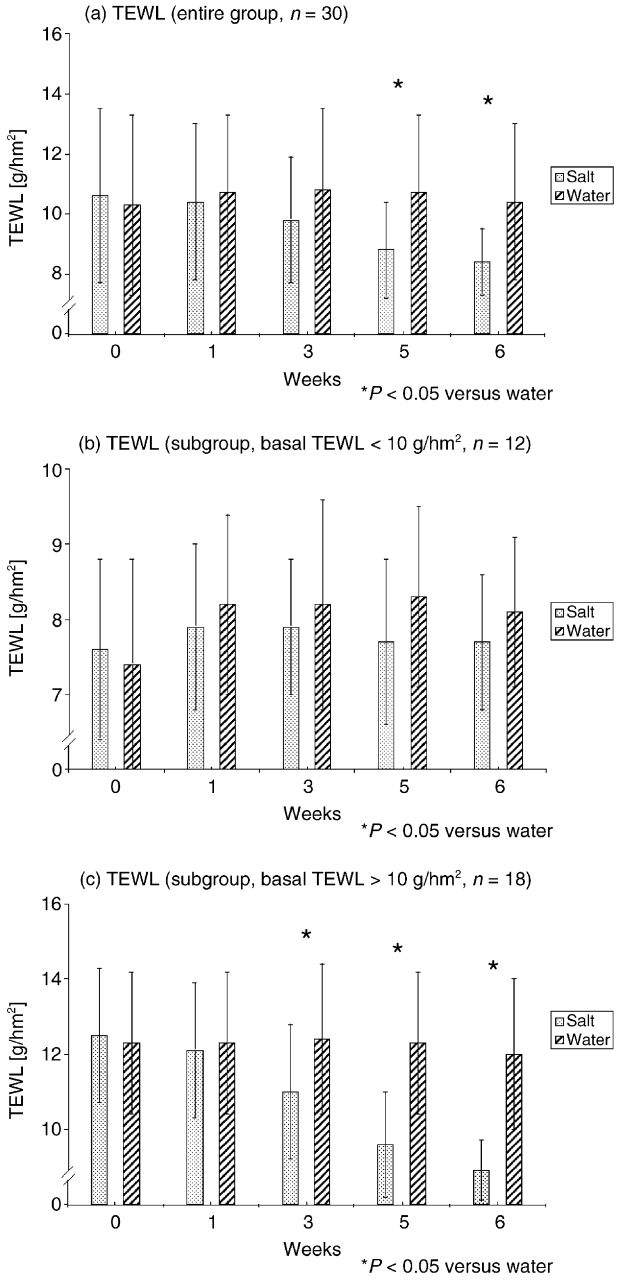

Figure 1 Variation of transepidermal water loss (TEWL) values in volunteers with atopic dry skin who submerged their forearm (daily for 6 weeks) for 15 min in a bath solution containing 5% salt of the Dead Sea. The control forearm was submerged in tap water only. Transepidermal water loss was recorded before the study (basal level, week 0) at weeks 1, 3, 5, and 6. Transepidermal water loss values are presented for (a) the entire group, (b) a subgroup with normal basal TEWL (nTEWL, TEWL < 10 g/hm²), and (c) a subgroup with elevated TEWL (eTEWL, TEWL > 10 g/hm²)

already achieved in 3 weeks. These results show that bathing with the magnesium-enriched Dead Sea salt solution significantly improved the barrier function of the skin.

Stratum corneum hydration

Next, we determined skin hydration, because reduced water content of the stratum corneum is the hallmark of dry skin. The use of the Dead Sea salt bath solution led to a slight increase in stratum corneum hydration after 6 weeks of treatment in the entire group and in both subgroups. After bathing in tap water a slight reduction in skin hydration occurred. Compared with the tap water-treated forearm side, a slight but significant increase in skin hydration for the entire group (+14%, $P < 0.05$) and the subgroups occurred on the Dead Sea salt-exposed side after 6 weeks of treatment (Fig. 2a–c). Therefore, regular bathing in high magnesium Dead Sea salt-containing solution significantly moisturizes the skin.

Skin roughness

A significant decrease in skin roughness at the salt-exposed forearm occurred after 3 weeks of treatment and further continued until the end of the study (after 6 weeks: –40%, $P < 0.05$). A slight decrease in skin roughness was also noticed on the tap water-treated side. Compared with tap water a significant reduction in skin roughness was found at the salt-exposed sides at 3, 5, and 6 weeks (Fig. 3a–c). This was true for the entire group and both subgroups, nTEWL and eTEWL. These results point to favorable effects of the Dead Sea salt solution on skin roughness, demonstrating that the salt smoothes the skin.

Skin redness (inflammation)

A significant decrease in skin redness was found after 6 weeks of treatment with the salt solution in the entire group and in the subgroup with nTEWL. A slight nonsignificant reduced redness was found in the subgroup eTEWL with elevated basal TEWL. In contrast, skin redness was unchanged after bathing with tap water. In comparison with the controls a significant decrease in skin redness occurred after 6 weeks of salt treatment in the entire group and the subgroup nTEWL with the subjects showing normal TEWL before the study. In the subgroup eTEWL there was also a tendency for a reduction in redness (not significant) (Fig. 4a–c). The results reveal a decrease in inflammation by bathing in the salt solution as shown by a reduced redness of the skin. It also indicates that bathing in the salt solution is well tolerated and does not irritate the skin.

Discussion

The effectiveness of bathing in Dead Sea salt solution to treat psoriasis is well known. In atopic dermatitis bathing in the Dead Sea itself may lead to burning because of the high salt

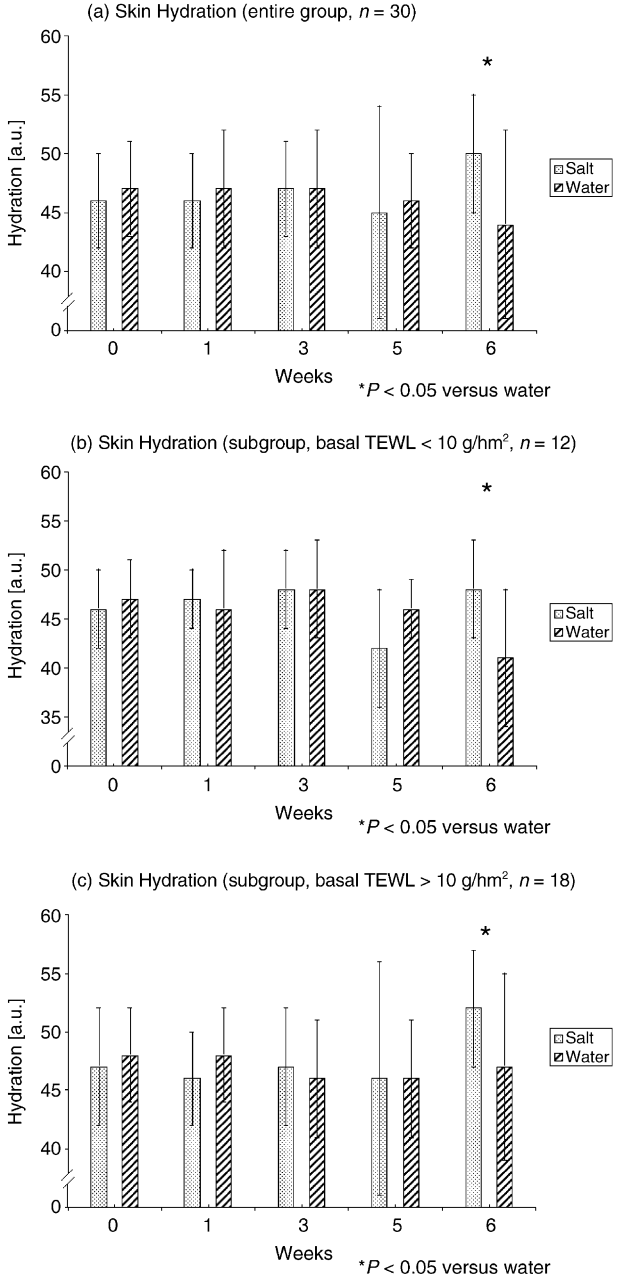

Figure 2 Variation of skin capacity as a marker for stratum corneum hydration. Treatment was performed and subgroups were used as described for Figure 1. Hydration was recorded in arbitrary units)

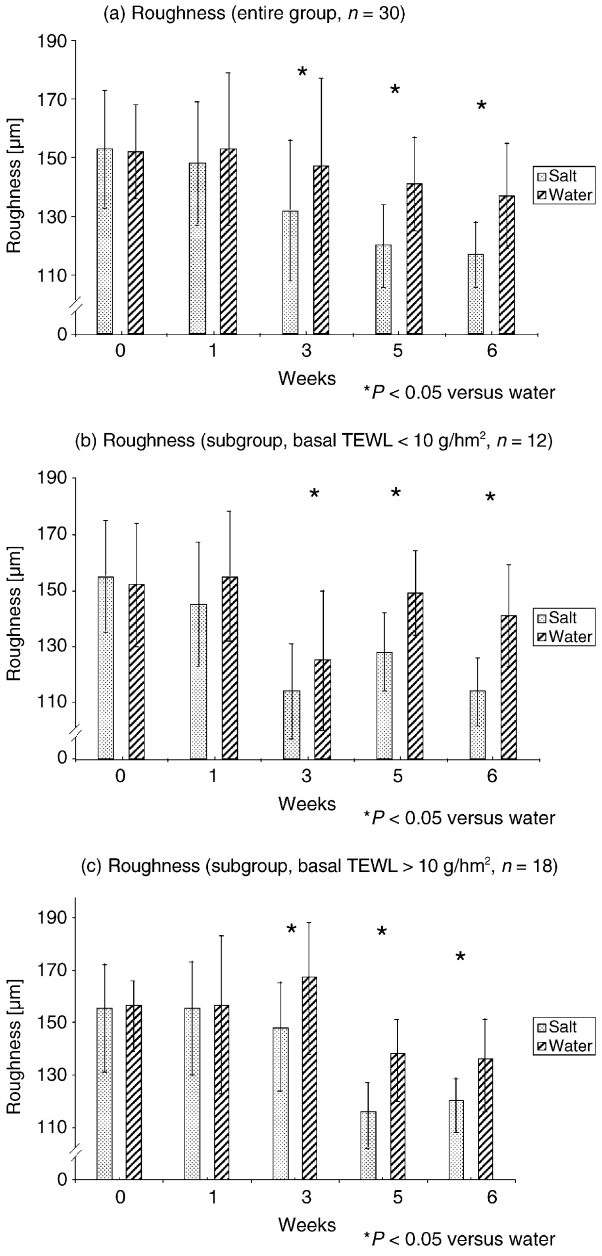

Figure 3 Variation of skin roughness. Treatment was performed and subgroups were used as described for Figure 1. Skin roughness was recorded as parameter Rz

content. Therefore, dilutions of Dead Sea salt water are used. We have shown here that a solution with 5% Dead Sea salt improved atopic dry skin. This is surprising, because each time the skin is washed, a temporary loss of skin moisture and a transient impairment of barrier function occurs, because the washing solution removes skin lipids and water-binding compounds. Frequent washing may lead to dry skin. Our study showed that exposure to tap water did not significantly influence biophysical parameters of the skin. The described aggravation of dry skin by washing is therefore related to the use of detergents.[25–29] Bathing in a Dead Sea salt solution containing a high amount of magnesium ions significantly improved atopic dry skin as was shown by biophysical parameters.

The existence of a defect in skin permeability barrier function in atopic dermatitis is well known. The extent of the

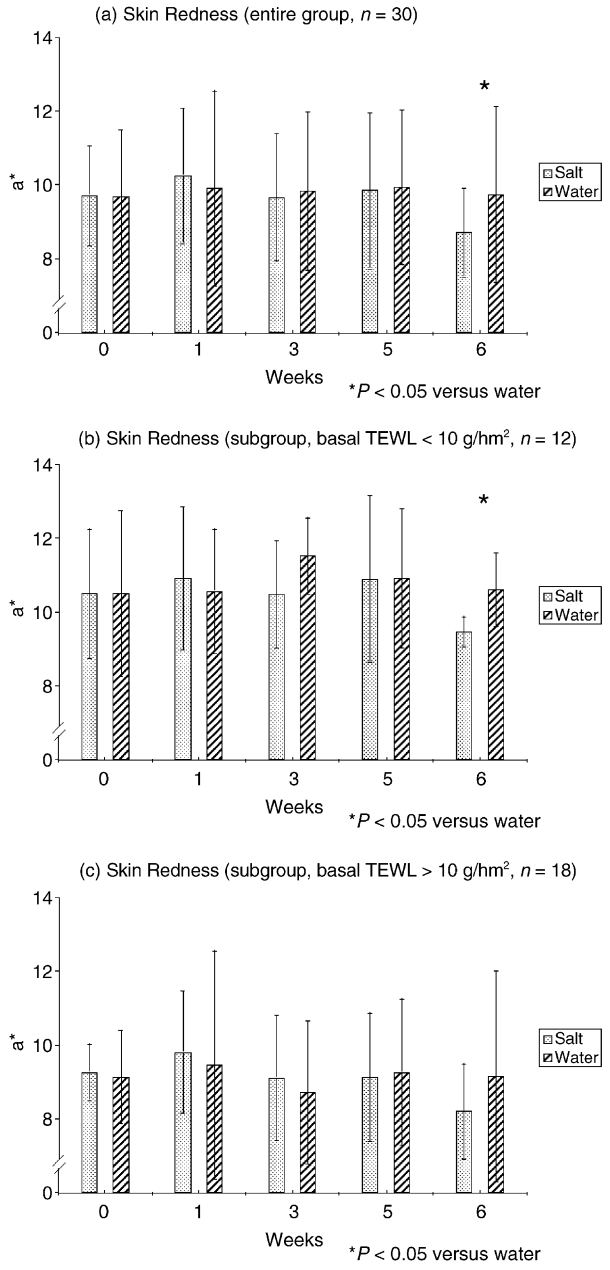

Figure 4 Variation of skin redness as a marker for inflammation. Treatment was performed and subgroups were used as described for Figure 1. Skin redness was determined as the a* value (red-green axes)

barrier abnormality correlates with the degree of inflammation.[21–24,30] Transepidermal water loss levels and the stratum corneum water content in completely healed patients are not different from normal controls.[24,31,32] We found in 12 of our 30 subjects with atopic dermatitis a normal TEWL comparable to that of healthy subjects (subgroup nTEWL). Eighteen volunteers showed elevated TEWL (subgroup eTEWL). After treatment with the Dead Sea salt solution skin barrier function was improved overall. But, when we divided our volunteers into the two subgroups, we found that only the subgroup eTEWL with an elevated TEWL before the study showed a significant reduction in TEWL. Tap water did not influence skin barrier function. This demonstrates that the elevated TEWL in this subgroup of volunteers can be normalized by bathing in a solution of magnesium chloride-rich Dead Sea salt in comparison with bathing in tap water. Understandably, in the subgroup with normal basal TEWL (nTEWL) no changes occurred.

The mechanisms for this improvement are only known in part. We have previously shown that dry skin is characterized by an enhanced proliferation and an impaired differentiation.[33] Ion concentration regulates skin permeability repair after artificial disruption.[34] Dead Sea salt may improve skin barrier function owing to the high content of magnesium ions along with calcium, which influence epidermal proliferation and differentiation.[34,35]

Bathing in the Dead Sea salt solution enhanced stratum corneum hydration. Hydration is important for the flexibility of the skin. Reduced hydration leads to dry skin characterized by a reduced elasticity, roughness, and scaliness. Dry skin may develop into eczema, followed by bacterial super-infection. In the present study we showed that the magnesium-rich Dead Sea salt containing bath solution not only prevented a loss in skin moisture content but also led to a significant increase in stratum corneum hydration. It is well known that magnesium salts are hygroscopic and bind water in the crystal lattice. Possibly, magnesium ions may be present in the extracellular spaces of the stratum corneum and may bind water by physicochemical effects. More likely, magnesium ions may regulate epidermal proliferation, differentiation, and barrier function thus influencing stratum corneum hydration indirectly.[36]

Skin roughness was reduced by both bathing with the tap water and the salt solution, but significantly more with the Dead Sea salt solution. Common bathing removes scales from the skin and this reduces skin roughness. The additional effect of the Dead Sea salt is most probably related to the influence of the salt solution on proliferation and differentiation.

Inflammation, determined by redness of the skin, was significantly reduced by bathing with the Dead Sea salt, but not by tap water. In general, inflammation is viewed as a consequence of the well-known immunological abnormalities of atopic dermatitis. Skin barrier defect is viewed as a consequence of the inflammatory phenotype.[24] We recently proposed that disturbed barrier function as a result of changes in lipid content and epidermal differentiation, may also be important for the pathogenesis of atopic dermatitis[32]. As a consequence of alterations in barrier function, aeroallergens grass pollen, birch pollen, cat dander, and house dust mite can penetrate the skin more easily, thereby perpetuating

eczematous lesions and inducing inflammation. We here suggest that bathing with Dead Sea salt improves barrier function and thereby indirectly reduces inflammation because of reduced penetration of harmful substances into the skin. But, there also may be a direct effect. Previously, it was found that magnesium ions exhibit anti-inflammatory properties,[11] inhibit contact dermatitis,[12] and the antigen-presenting capacity of Langerhans' cells.[13]

The distribution of ions in the skin is of importance. In normal skin, magnesium and calcium ions were localized with a high concentration in the upper epidermis. After barrier disruption, the gradients of calcium, magnesium, and potassium in the epidermis disappeared while the pH was not altered.[35] Loss in the ion gradient is a signal for an increase in proliferation, differentiation and lipid synthesis aimed to repair the perturbed barrier.[34]

Denda *et al*. found that a magnesium chloride solution containing calcium chloride accelerated barrier repair more effectively than a solution of magnesium chloride alone.[35] Dead Sea salt contains high concentrations of magnesium ions in the presence of calcium.

In summary, we found that bathing with Mavena® Dermaline Mg[46] Dead Sea salt solution, owing to its high content of magnesium ions, enhanced stratum corneum hydration, improves skin barrier function and reduces skin roughness and inflammation.

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