

The treatment of atopic eczema with Dermagiq Skin® ointment

Dr M.W.H.M. Roovers and Dr I. Boersma

Introduction

According to information published by the Dutch National Institute for Public Health and The Environment (RIVM) in the National Public Health Compass 2007, the annual prevalence rate of atopic eczema in the Netherlands is 14.8-17.5%. Although atopic eczema affects all age groups, it occurs predominantly in young children. Objective (i.e. visible) symptoms include erythema, oedema and excoriation. Many patients also experience symptoms such as itching and sleeplessness that impact significantly on the quality of their lives. Because eczema can be severely itchy, it is almost impossible to suppress the urge to scratch. While scratching offers some relief, the itch returns quickly and the skin has been further damaged in the process. As a result, the eczema becomes worse and skin infections can occur that may be accompanied by infected wounds and scabs.

If the eczema symptoms are really severe, the GP will refer the patient to a dermatologist or allergologist. The medication offered often incorporates a neutral ointment base (cetomacrogol cream, paraffin/silicone cream, etc.) in order to improve the condition of the skin, and an anti-inflammatory salve and medicines to suppress the itchiness. In many cases, the patient is prescribed a corticosteroid ointment. One disadvantage of corticosteroids is that they can make the skin thin and oversensitive, while the anti-inflammatory effect can mean that a bacterial or fungal infection will go unnoticed and can therefore worsen. Used properly, the side-effects of creams containing corticosteroids may be minimal, but patients and the parents of young children are often reluctant to use creams containing these compounds. There is therefore a clear need for a product that can tackle the symptoms of eczema without the aid of corticosteroids. This article describes the characteristics and clinical results of an ointment based on antibacterial and anti-inflammatory honey.

Honey as active ingredient

Specific types of honey have long been known for their wound-healing properties (Molan et al., 1992, 2001, 2006). In collaboration with Wageningen University, a type of honey has been developed that combines unusual wound-healing, antibacterial and anti-inflammatory properties. This honey is produced under controlled conditions, so that its ingredients are very consistent and its bioactivity is high. The antibacterial effect comes from natural enzymes in the honey, and the anti-inflammatory effect comes from plant-based antioxidants. Because of the presence of gluconic acid, the honey has a low pH value (4.0). This enzyme-rich honey (Revamil®) is used in products sold for purposes such as wound healing and vaginal infections (Creemers et al., 2005, Creemers and Bosma, 2006, Eijk and Groenhart, 2006). The antibacterial effect of Revamil® on the skin flora was demonstrated in a clinical study at the Amsterdam Medical Center (Kwakman et al., 2008). That study showed that colonisation of the skin declines by a factor of 100 when Revamil® honey is applied to the skin over a period of two days.

Dermagiq Skin® ointment

Dermagiq Skin® ointment contains a basic skin care cream in combination with enzyme-rich honey that has been produced under controlled conditions. Dermagiq Skin® ointment

contains no corticosteroids and has a low pH value (4.5-5), which corresponds precisely with the pH value of healthy skin. The bioactive honey used in Dermagiq Skin® ointment provides an effective antibacterial and anti-inflammatory effect. Dermagiq Skin® ointment is a safe, CE registered product (class 2a) for the treatment of eczema and superficial wounds.

The antibacterial effect of honey

Bees add the glucose oxidase (GOX) to honey and this enzyme activates the conversion of honey sugar (glucose) into gluconic acid and hydrogen peroxide (Kerkvliet 1996, Inés et al., 1997). The enzyme remains intact - but inactive - in partially ripened honey, but as soon as a little moisture is added, such as on the skin or in a wound, it becomes active again (Figure 1).

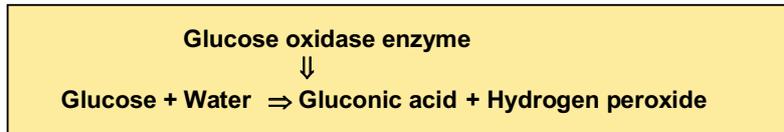


Figure 1. Conversion of honey sugar (glucose) by the enzyme glucose oxidase gives rise to the slow release of small amounts of hydrogen peroxide and ensures that the resulting gluconic acid has a low pH value.

One measure of enzyme activity is the amount of hydrogen peroxide that is produced in diluted honey per unit of time (Kerkvliet, 1996). Figure 2 shows a comparison of the peroxide production over time between the controlled enzyme-rich honey that is used in Dermagiq Skin® and a representative sample of table honey. The enzyme level in the controlled Dermagiq Skin® is significantly higher than that in table honey, and the enzyme is effective for a longer period (76 hours versus 19 hours).

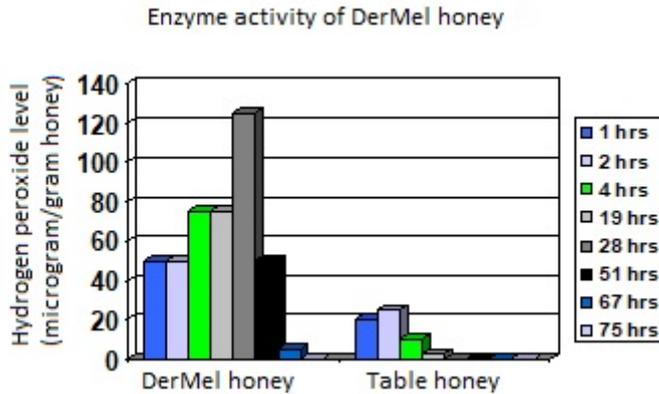


Figure 2. Enzyme activity in Dermagiq Skin® and table honey (acacia) shown as the amount of hydrogen peroxide that is produced per gram of honey.

In order to demonstrate the antibacterial effect of Dermagiq Skin® ointment, a Challenge Test was carried out with *Staphylococcus aureus* and *Pseudomonas aeruginosa*, two bacteria that frequently cause skin infections. In this Challenge Test, one million bacteria per gram of honey are added at time point zero. Samples are subsequently taken at various time intervals in order to determine the number of surviving bacteria present in the honey. The results of the Challenge Test (carried out in accordance with the European Pharmacopoeia) demonstrate that there were no more live bacteria to be found in the Dermagiq Skin® ointment after 24 hours (Figure 3). One important result was that the multiresistant *Staphylococcus aureus*

(MRSA) was also killed off just as quickly by Dermagiq Skin® as the antibiotic-sensitive MSSA strain.

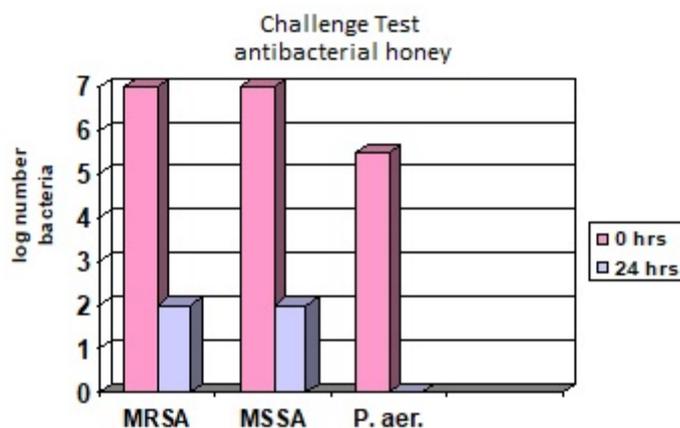


Figure 3. Challenge Test of antibacterial honey against methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-sensitive *Staphylococcus aureus* (MSSA) and *Pseudomonas aeruginosa*.

Anti-inflammatory properties of honey

Honey's anti-inflammatory properties can partly be explained by the presence of flavonoids originating from flowers (Siess et al., 1996). Flavonoids have strong antioxidant properties and remove harmful oxygen radicals. The medicinal honey that is used in Dermagiq Skin® ointment has been tested for antioxidant activity. For this purpose, human leukocytes were encouraged to produce oxygen radicals. Subsequently, a chemiluminescence assay was used to determine the concentration of honey involved in slowing down the production of oxygen radicals. From the test it was evident that a honey concentration of just 1.6% produced a 50% reduction in the production of oxygen radicals.

Survey of patient experience

A survey of patients – based on the Three Item Severity (TIS) score - was carried out at two different hospitals using DerMel® ointment¹ (Wolkerstorfer, 1999). A total of 24 patients at the Amphia Hospital in Breda and the St. Elisabeth Hospital in Tilburg took part in the survey. All the patients had atopic eczema, nearly all of them had objective symptoms on the face and other parts of the body.

The patients continued to take any medication they were taking at the beginning of the survey, but after the first visit to the doctor any use of another ointment base was ceased and replaced by treatment with the DerMel® ointment.¹ The patients subsequently visited the doctor again for a second and third time, on average at two and a half week intervals. The scores for objective symptoms (erythema, oedema and excoriation) and subjective symptoms (itchiness, sleeplessness) were noted by the doctor at each visit. During the third visit, the patients were also asked to score their overall experience on a scale of 0 to 10.

Results of the survey

¹ The survey was carried out using DerMel®; the composition of Dermagiq Skin® is identical.

The ages of the patients ranged from 8 months to 57 years of age (Figure 4).

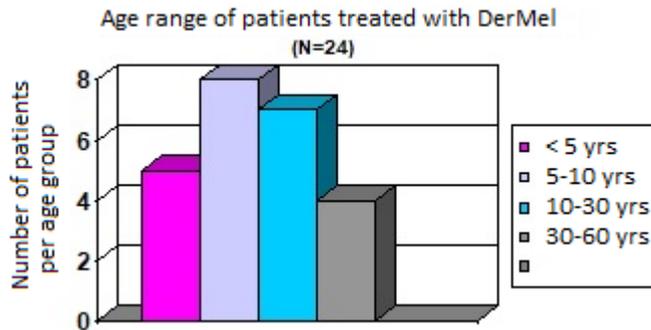


Figure 4. Age range of patients treated with DerMel® ointment (identical to Dermagiq Skin®).

Objective symptoms

Treatment with DerMel® ointment (identical to Dermagiq Skin®) led to a reduction of erythema and excoriation in 18 of the 24 patients (Figure 5a). Two to three weeks after commencing the treatment with DerMel® ointment, the erythema and excoriation had been reduced from moderate to mild (Figure 5b). In the case of one patient, the erythema worsened during the first two weeks and the treatment was ceased. During the first visit to the doctor, 18 of the patients had moderate to mild oedema; for 7 of these patients, the treatment with DerMel® ointment resulted in a reduction of the symptoms. The largest reduction of symptoms as a result of the treatment with DerMel® ointment was achieved after just two to three weeks.

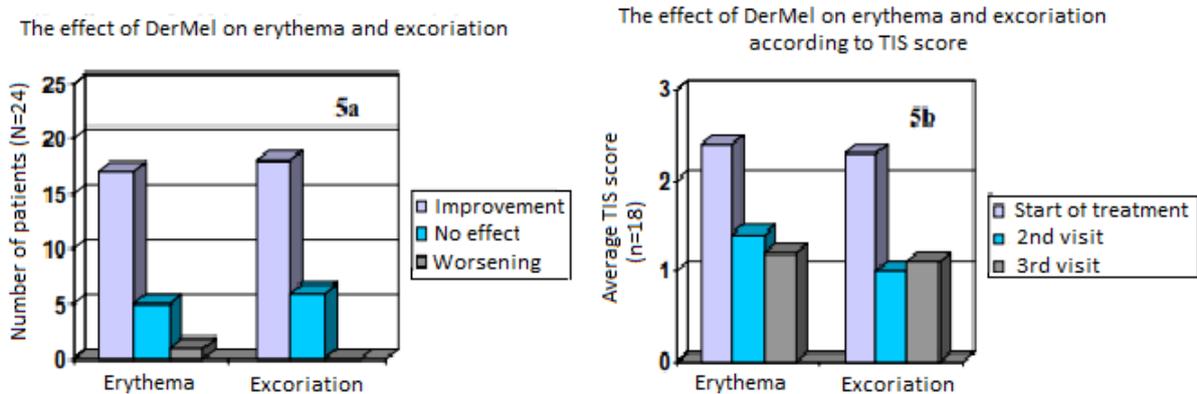


Figure 5. The effect of DerMel® ointment on erythema and excoriation. 5a: Number of patients who experienced some or no improvement, or a worsening of the symptoms. 5b: TIS score (0 = none, 1 = mild, 2 = moderate, 3 = severe) for patients who responded positively to the treatment with DerMel® ointment.

Subjective symptoms

For 20 of the 24 patients, treatment with DerMel® ointment led to a reduction of itchiness, and 18 reported less trouble sleeping (Figure 6a). On a scale of 0 to 10, itchiness reduced on average from 8 to 4, and sleeplessness from 3 to 1. As with the objective symptoms, a significant reduction of itchiness and sleeplessness also occurs after the DerMel® ointment has been used for just two to three weeks.

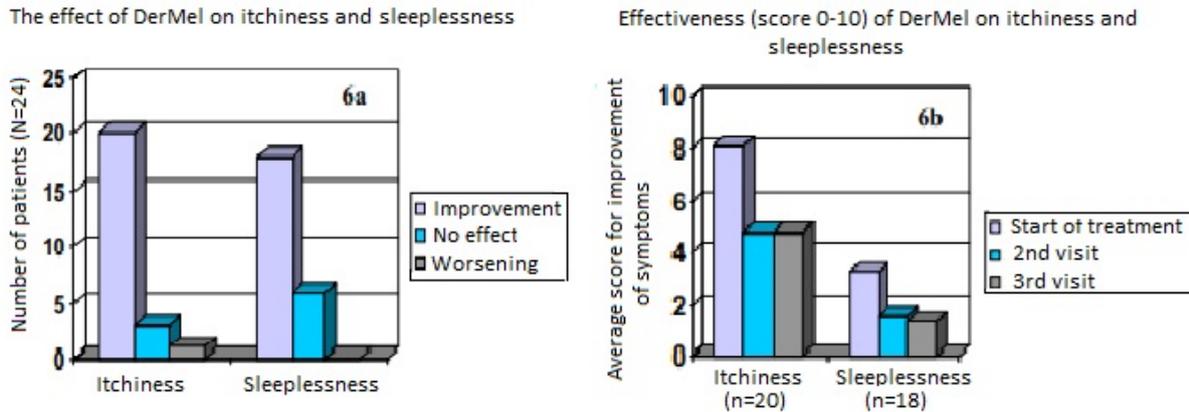


Figure 6. The effect of DerMel® ointment on itchiness and sleeplessness as a result of having atopic eczema.

6a: Number of patients who experienced some improvement, none, or a worsening of the symptoms.
 6b: Overall score of patients who responded positively to the treatment with DerMel® ointment (0 = none, 10 = very positive).

Experience of patients

The majority of the patients were very positive about the effectiveness of DerMel® ointment. Figure 7 shows a summary of the patients' own assessment of the effectiveness of DerMel® ointment. Nineteen patients found DerMel® ointment to be effective. Some of the comments from patients: According to the mother of a 7-year-old patient: "This is the best ointment we've ever had"; 25-year-old patient who has been using hydrocortisone cream for 22 years: "very satisfied" and "it also works for folliculitis barbaris"; Parents and 11-year-old patient: "very satisfied".

Three patients experienced no improvement to their symptoms as a result of using DerMel® ointment; two of them found the ointment to be 'sticky'. Two patients were dissatisfied: one patient reported that the ointment stung on application, the other patient experienced a worsening of the redness of the skin.

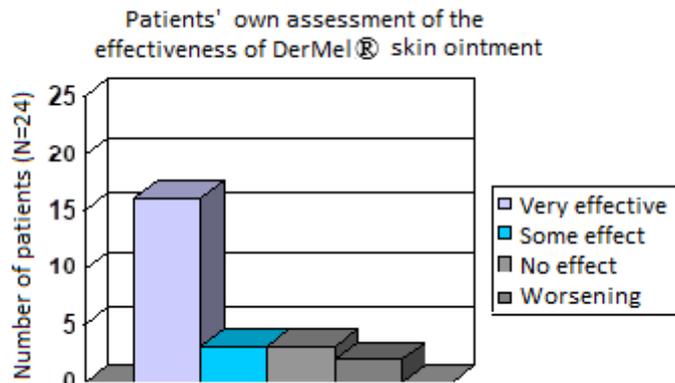


Figure 7. Patients' assessment of the effectiveness of DerMel® ointment.

Conclusions

From the survey of patients' experiences, it transpires that DerMel® ointment (which is identical to Dermagiq Skin® ointment) alleviates the symptoms of atopic eczema in the majority of patients. The main symptoms that are lessened are erythema, excoriation, itchiness and sleeplessness. Just like Dermagiq Skin®, DerMel® ointment combines the anti-inflammatory, antibacterial and wound-healing properties of honey with the skin care properties of a neutral basic ointment. Very few people are sensitive to this ointment and it can therefore be used even on the most sensitive of skins. Dermagiq Skin® and DerMel® ointment proved to be good alternatives for various other ointment bases, and they can easily be combined with other dermatological medication.

Literature consulted

(Sources with translations added in italics are only available in Dutch)

- Creemers T, Bosma WJ, Boon ME. Enzymrijke honing: een natuurlijke remedie voor vaginale dysbalans [*Enzyme-rich honey: a natural remedy for vaginal imbalance*]. Annual Report of the Leiden Cytological and Pathological laboratory, 2005.
- Creemers T, Bosma WJ. Honingzalf voor wondgenezing en huidproblemen bij dieren [*Honey ointment for wound healing and skin problems in animals*]. Dier en Arts [*Animal And Vet*], 2006. volume 21, no. 4.
- Eijk W van and Groenhart O. Zoet na het zuur. Revamil honinggel, een goede remedie voor wonden [*Sweet after sour. Revamil honey gel, a good remedy for wounds*]. 2006; WCS Newsletter 22(4): 6-10
- Inés Mato, José F. Huidobro,* M. Pilar Sánchez, Soledad Muniategui, Miguel A. Fernández-Muiño, and M. Teresa Sancho. Enzymatic Determination of Total D-Gluconic Acid in Honey. J. Agric. Food Chem. 1997; 45 (9): 3550 -3553.
- Kerkvliet JD. Screening method for the determination of peroxide accumulation in honey and relation with HMF content. J. Apicult Res 1996; 35: 110-117
- Kwakman PHS, Van den Akker JPC, Güçlü A, Aslami H, Binnekade J, de Boer L, Boszhard L, Paulus F, Middelhoek P, te Velde A, Vandenbroucke-Grauls CMJE, Schultz MJ, SAJ Zaat. Medical grade honey kills antibiotic-resistant bacteria in vitro and eradicates skin colonization. Accepted for publication in "Clinical Infectious Diseases"
- Molan PC. The antibacterial activity of honey. 2. Variation in the potency of the antibacterial activity. Bee World 1992; 73(2): 59-76.
- Molan PC. Why honey is effective as a medicine. 2. The scientific explanation of its effects. In: Honey and Healing, 2001, Munn P and Jones (eds), International Bee Research Association (IBRA), pp 14-26.
- Molan PC. The evidence supporting the use of honey as a wound dressing. Lower Extremity Wounds 2006; 5(1): 40-54.
- Nationaal Kompas Volksgezondheid [*National Public Health Compass*], version 3.12, 13 December 2007. Compiled by RIVM Bilthoven.
- Siess MH, Le Bon AM, Canivenc-Lavier MC, Amiot MJ, Sabatier S, Aubert SY, Suschetet M. Flavonoids of Honey and Propolis: Characterization and Effects on Hepatic Drug-Metabolizing Enzymes and Benzo[a]pyrene-DNA Binding in Rats. J. Agric. Food Chem. 1996; 44 (8): 2297 -2301
- Wolkerstorfer A, De Waard-van der Spek FB, Glazenburg EJ, Mulder PG, Oranje AP. Scoring the severity of atopic dermatitis: three item severity score as a rough system for daily practice and as a pre-screening tool for studies. Acta Derm Venereol 1999; 79: 356-359.