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# Moisturizing effect of topical cosmetic products applied to dry skin

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**Synopsis**

One of the complications of "diabetes mellitus" is termed diabetic foot syndrome, the first symptoms of which include changes in the skin's condition and properties. The skin becomes dehydrated, dry, and prone to excessive formation of the horny layer, its barrier function becoming weakened. This function can be restored by applying suitable cosmetic excipients containing active substances. The aim of this study was to evaluate and compare the effects of commercially available cosmetic products (CPs) designed for the care of diabetic foot, through a group of selected volunteers using noninvasive bioengineering methods. Statistical surveys ($p < 0.05$) evaluated these CPs as regards to their hydration effect and barrier properties. Special attention was devoted to CPs with the declared content of 10% urea, and that the influence of this preparation's ability to hydrate and maintain epidermal water in the epidermis was confirmed.

## INTRODUCTION

Diabetes mellitus (DM) belongs to a group of heterogeneous diseases. The World Health Organization defines DM as a state of chronic hyperglycemia, which may be caused by a number of exogenous and endogenous factors acting simultaneously. The clinical course of each type of DM is highly variable, but a single common characteristic is the presence of hyperglycemia, which occurs on the basis of insufficient action of insulin in the tissues. Abnormalities, however, occur in the metabolism of fat and protein as well, in addition to those in electrolyte and water management of the body (1–3). DM, like other endocrine disorders, may be the cause of changes in the function and properties of the skin. Skin complications occur in approximately 30% of patients and may also be the first sign of DM. Hyperglycemia and reduced insulin are factors involved in deterioration of skin function, causing the skin of patients with DM to decrease hydration capacity, in addition to reducing the activity of the sebaceous glands (4,5). DM causes glycosylation products

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in the collagen contained in the dermis to increase. Furthermore, the abnormal proliferation and differentiation of keratinocytes in the epidermis can be assumed to have effects on the function of the stratum corneum (SC) in patients with DM. The response to mechanical stresses is plantar SC hypertrophying; such stresses potentially being a high-risk factor for ulcerations to develop in persons suffering from DM (6–15). A number of publications dedicated to skin changes in DM exist (16–24).

For patients with DM, the skin suffers from the lack of lipids supporting skin hydration, with injuries caused due to dry skin potentially leading to infections or even diabetic foot syndrome. Caring for dry skin on the foot is one of the basic recommendations of educational activities conducted for people with diabetes. Feet should be inspected and bathed on a daily basis, carefully dried after a bath, especially between the toes, and oiled using a greasy ointment or moisturizer (5,20,21,25–28). The purpose of this basic foot care is to improve or preserve the skin's elasticity. A rule of thumb for diabetic foot states that preventing defects is better than healing them subsequently. Ideal skin moisturizers not only soften the skin, but also create a protective film on its surface and in terms of physiology, limit transepidermal water loss (TEWL). The extent of such an effect depends on the overall composition of the applied preparation (29,30). Substances possessing these properties may include, for instance, urea or glycerol. According to some authors (31–37), glycerol-containing creams dispose of similar clinical effect as urea-based creams. Glycerol and urea easily penetrate into SC and enhance its capacity of water uptake. These studies also suggest that suitable urea-containing formulations can favor more barrier properties.

This study deals with monitoring the declared hydration effects of six commercial cosmetic products (CPs) designed for the care of diabetic foot, the same employing corneometric methods and determining TEWL. It has been declared by the producers of the moisturizers under test that the CPs were designed especially for people with diabetes to take daily care of dry and cracked skin of the foot, for skin regeneration and intense moisturizing, softening, and restoring, or enhancing the skin's barrier function. The humectants that all the preparations chiefly utilize are glycerol and urea, in varying proportions. For Eucerin® (cream) and Allpresan® (foam), the producer declared a 10% urea content. The moisturizing effects of the tested products were compared with a prepared ointment base, lacking the active substances mentioned earlier.

## EXPERIMENTAL PART

### GROUP OF VOLUNTEERS

The process of selecting volunteers and the testing procedure followed the principles enshrined in the International Ethical Guidelines for Biomedical Research Involving Human Participants (38). The study included 22 women (N = 22) aged 45 ± 8 years. All the female volunteers met the criteria for inclusion in the study, completed a study participation questionnaire and signed an informed consent form to participate in the study. None of the persons withdrew from the study before its completion. The female volunteers were instructed to avoid applying any CPs to any application area 12 h before and throughout the test; only an evening shower with water was permitted. Measurements were taken in an air-conditioned room (temperature 24 ± 2 °C, relative humidity of 60 ± 4%); temperature of the skin of volunteers was 33.2 ± 0.7°C.

### INSTRUMENTAL TECHNIQUES

The procedure for SC hydration measurement involved the CORNEOMETR® CM 825 (Courage & Kazaka Electronic GmbH, Cologne, Germany). In principle, the instrument assesses changes in the electrical capacity of the skin's surface that indicates SC hydration. The parameter depends on the value of the dielectric water constant, relative to other elements of the skin. The Corneometer gives only a relative assessment of skin hydration (39). For TEWL (40), as an indicator of successful skin barrier function, the authors used the TEWAMETER® TM 300 (Courage & Kazaka Electronic GmbH). One of the most accurate procedures, this method can detect even the slightest disruption of skin barrier function. It is based on the diffusion of water into the area of an open chamber of cylindrical shape while determining the density gradient between two pairs of sensors (temperature and relative humidity). Digital imaging was used to evaluate physiological changes in the skin and to obtain photographic documentation, employing a VISIOSCOPE COLOR® (Courage & Kazaka Electronic GmbH) video magnifier.

### MATERIALS AND METHODS

A total of six cosmetic moisturizers (five creams and one foam, n = 6) designed for diabetic foot were tested along with the prepared ointment base without effective moisturizing agents (Table I). The tested CPs for diabetics indicate composition according to the International Nomenclature of Cosmetic Ingredients (INCI). It was claimed that the Beline® balm would oil dry skin, bind moisture, improve blood circulation, and prevent skin inflammation, in addition to having nourishing and regenerative properties. Beline is a special caring CP for strong-stressed legs and feet with a strong healing effect. It is made on herbal base containing urea, panthenol, allantoin, chamommila, and other flower extracts. Nourishing and regenerating properties were declared for the Ziaja® cream, including supporting the strengthening of the skin structure and preventing cracks in the same. Active substances include hydroxyproline to firm the skin and other additives for conditioning and regenerating the skin such as hydrolyzed lupine protein, oligopeptides (collagen), and oligosaccharides. Eucerin® cream was designed for extra dry and cracked skin on both legs and feet and is recommended by the manufacturer for complementary care in the dermatological treatment of not only the skin of the feet of diabetics but also atopic eczema, psoriasis, and ichthyosis. Along with 10% urea, which helps accelerate the elimination of a thickened horny layer and regeneration of the skin, an additional active moisturizing ingredient was used, specifically lactic acid that effectively binds water in skin cells. For Allpresan® foam, the moisturizing effect of 10% urea was supported by Pentavitin® (a commercial name of carbohydrate complex) and panthenol. The foam contained no aromatics and preservatives. DiabeCare® was a product specially developed for the dry and sensitive skin of diabetics. It contains a combination of selected active substances with a fully ranging action on hydration and regeneration of the skin. The Scholl® cream is declared to stimulate the skin by renewing cells in rough, dry, and cracked skin.

Before actually applying the cosmetics to the skin, pretreatment of the skin was performed on eight areas of the left and right hands on the sides of the volar forearms using a 0.5% solution of sodium laurylsulfate (SLS) in saline solution for 4 h. SLS solution of 0.5% was used to clean and degrease the skin with the view to eliminate individual factors.

**Table I**
Composition of the CP for Foot Care Designed for Diabetics According to the INCI

| CP | Composition |
|---|---|
| Beline® (cream) | Aqua, Ethylhexyl stearate, Hydrogenated palm glycerides, Caprylic/Kapric triglyceride, Glycerine, Cetearyl alcohol, Ceteareth-100, Glyceryl stearate, Butyrospermum parkii, Zea germ mays oil, Urea, Propylene glycol, Lanolin cera, Dimethicone, Ethoxidiglycol, Panthenol, Allantoin, Phenoxyethanol, Iodopropynyl butylcarbamate, Calendula officinalis flower extract, Equisetum arvense extract, Chamommila recutita flower extract, Niacinamide, Benzyl nicotinate, Methylparaben, Propylparaben, Ethylparaben, Butylparaben parfum |
| Ziaja® (cream) | Aqua, Glycerine, PPG-15 Steraryl ether, Elaeis guineesis (palm) oil, Steareth-2, Steareth-21, Cetyl alcohol, Methylsilanol hydroxyproline aspartate, Dimethicone, Polyacrylamide, C13-14 Isoparaffin, Laureth-7, Panthenol, Hydrolyzed lupine protein, Lecithin, Urea, Tocopheryl acetate, Sodium polyacrylate, Phenoxyethanol, Methylparaben, Propylyparaben, 2-Bromo-2-nitropropane-1,3-diol, Diazolidinyl urea, Cymbopogon schoenanthus oil, Citral, Geraniol, Citric acid |
| Eucerin® (cream) | Aqua, Glycerine, Urea, Cetearyl alcohol, Sodium lactate, Caprylic/Capric triglyceride, Ethylhexyl cocoate, Hydrogenated coco-glycerides, Octyldodecanol, Cera microcristallina, Paraffinum liquidum, Dimethicone, Sorbitan stearate, Aluminum starch octenylsuccinate, Lactic acid, Phenoxyethanol, PEG-40 castor oil, Sodium cetearyl sulfate, Carbomer |
| Allpresan® (foam) | Aqua, Urea, Butane, Decyl oleate, Octyldodecanol, Cetearyl alcohol, Propane, Stearic acid, Propylene Glycol, Glycerine, Glyceryl stearate, Panthenol, Sacharide isomerate, Undecyl alcohol, Allantoin, Potassium lauroyl wheat amino acid, Palm glycerides, Capryloyl glycine, Sodium lauroyl sarcosinate, Citric acid, Pentavitin made by Pentapharm Ltd |
| DiabeCare® (cream) | Aqua, Glycerine, Glyceryl stearate, Ceteareth-20, Ceteareth-12, Cetearyl alcohol, Cethyl palmitane, Parafinum liquidum, Urea, Cetearyl ethylhexanoate, Macadamia ternifolia seed oil, Panthenol, Synthetic beewax, Ceramide 3, Ceramide 6 II, Ceramide 1, Phytosphingosine, Cholesterol, Sodium lauroyl lactylate, Phenoxyethanol, Methylparaben, Butylparaben, Ethylparaben, Propylparaben, Isobutylparaben, Carbomer, DMDM hydantoin, Triethanolamine, Parfume, Tocopheryl acetate, Aloe barbadensis, α-Isomethyl ionone, Butylphenyl methylpropional |
| Scholl® (cream) | Aqua, Urea, Dimethicone, Decyl oleate, Petrolatum, Lanolin, Dicocoyl pentaerythrityl distearyl citrate, Cera microsristallina, Glyceryl oleate, Paraffin, Keratin, Hydrolyzed keratin, Panthenol, Aluminium stearate, Propylene glycol, Phenoxyethanol, Carbomer, Chlorphenesin, Bisabolol, Tocopheryl acetate, Sorbitol, Methylparaben, Butylparaben, Ethylparaben, Propylparaben, Isobutylparaben, BHA, Citric Acid, Sodium Phosphate, Faex, Potassium Sorbate. |
| Ointment base | Aqua purificata, Parafinum solidum, Parafinum liquidum, Alcohol cetylstearyl, Slovasol 2430, Trolaminum, Carbomerum 980, Methylparaben, Propylparaben |

This method is also an acceptable model for pretreatment of DM patients' skin. Only then there was a one-off application of the CPs, the volume being 0.1 ml for each, to six areas of 8 $cm^2$ each, as shown in Fig. 1. The ungreased area, not treated with a preparation, served as a control for any irritative effects. Experimental values for the monitored parameters after degreasing were obtained by measuring each characteristic at the time intervals of 0, 1, 2, 3, 4, 24, 25, and 26 h. The hydration measured, using the corneometric technique, was determined five times for each volunteer in each delimited area of the

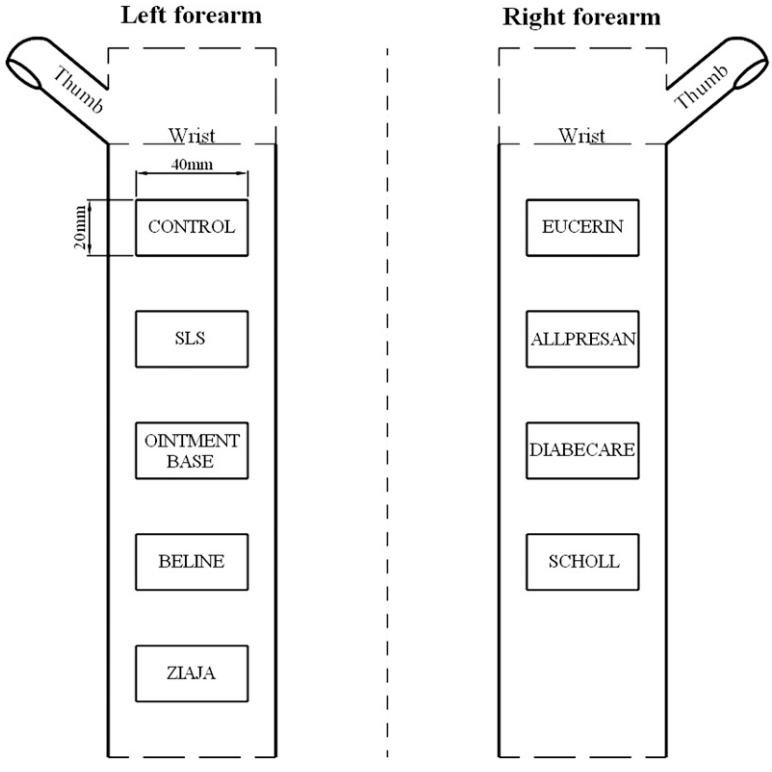


**Figure 1.** A diagram describing the tested area with CP application to the volar forearms on the left and right hands.

volar forearm. Since measurement of water evaporation from the skin is significantly related to the temperature of the skin cover, the environment, and the probe, measurements were carried out 15 times, with the first five values not included in the calculation of the arithmetic mean.

### STATISTICAL DATA PROCESSING

Calculating statistical data and creating graphical outputs were conducted using Excel 2010 and Statgraphics 6.0 (Manugistic, Inc., Rockville, MD). All the measured data were transferred to the database. Arithmetic means and standard deviations (SD) were calculated for the values obtained via corneometric measurement. Average hydration values acquired after pretreating the skin using SLS were subtracted from the mean CP hydration values, thus achieving the same initial conditions for each volunteer. Arithmetic means and SDs were calculated using the primarily obtained TEWL data as well. The baseline was the time prior to the actual action of applying each CP to the test areas of the volar forearms on the right and left sides of each participating volunteer. The analysis of variance (ANOVA) factor evaluation was used for CP application at each time (1, 2, 3, 4, 24, 25, and 26 h) and the mutual interactions of these. The significance level of 5% ($p < 0.05$) was chosen for statistical analysis. An F-test was carried out to discern the effects of CP containing 10% urea as declared against the control untreated area.

## RESULTS AND DISCUSSION

### COMPARISON OF THE HYDRATION EFFECTS OF THE TESTED CP AND OINTMENT BASE

Skin hydration was measured on pretreated skin, with the period within 24 h of application selected as a decisive interval for diagnosis of the action. The observed hydration effect for each CP was comparable (Fig. 2): Beline® 12.7 ± 6.5 c.j., Ziaja® 11.9 ± 7.4 c.j., Eucerin® 13.5 ± 7.7 c.j., Allpresan® 13.9 ± 7.2 c.j., DiabeCare® 15.3 ± 7.0 c.j., and Scholl® 16.5 ± 8.3 c.j. In contrast, the value of hydration shown for the ointment base without active hydration ingredients was at the level of pretreated skin. The negative hydration values for Scholl® just after application corresponded to the impenetrable film that it created and the imperfect penetration of the cream into the epidermis. The evidence of the occlusive film is shown in Fig. 3.

### COMPARISON OF TEWL WITHIN THE AREAS OF APPLICATION OF THE CP AND THE OINTMENT BASE

The results of TEWL measurement (Fig. 4; Table II) of the untreated control area exhibited a slight decrease over the measured time intervals compared with the baseline. When comparing the control area to those with the CP applied, a decrease was shown in TEWL values at the measurement times of 1, 2, 3, 4, 24, and 25 h, i.e., a positive effect of the products used on skin barrier function. The highest negative differences found were those after 4 h of exposure to CP, for Beline®, Ziaja® and DiabeCare® creams, and the Allpresan® foam. As regard the ointment base, the same was found after 4 and 25 h of its action on the skin. The Scholl® cream was found to have increased the TEWL value within 1, 3, and 26 h of action compared to the control surface. Values expressing an occlusive effect of the tested CP were reported only for the Scholl® cream and the ointment base used. For the

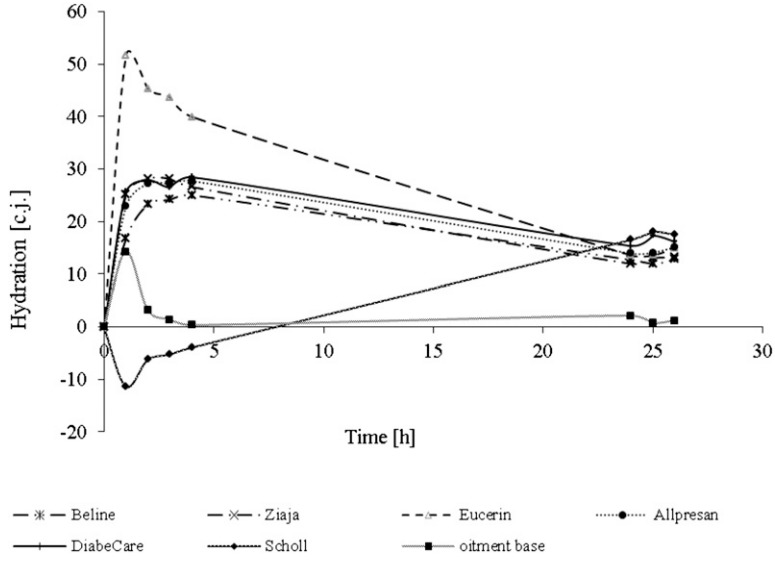


**Figure 2.** Corneometric measurements of skin hydration.

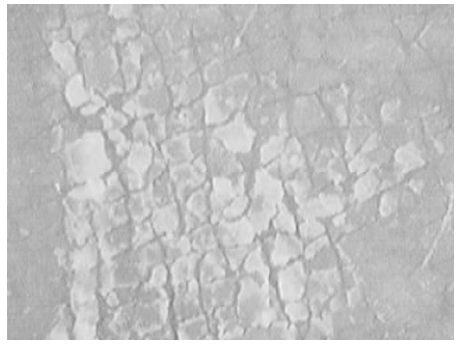

**Figure 3.** The occlusive film of the Scholl® cream (image captured on a Visioscope).

ointment base, the occlusion effect disappeared after 1 h of application to the skin, which for Scholl® occurred after 3 h of the cream's action. Statistical results from comparing the tested CP with the ointment base at each time interval (significance $p \leq 0.05$) were found and identified as * in Table II.

### COMPARISON OF THE HYDRATION EFFECT OF CP WITH THE DECLARED CONTENT OF 10% UREA

Furthermore, two different CPs with the declared content of 10% urea were subject to comparison for the effect of hydration, including Eucerin® and Allpresan®, and investigated corneometrically. Both of the products contained other active moisturizing agents. F-tests were carried out to discern the effects of these two products against the control untreated area. For Eucerin®, increased hydration was shown to be significant at time

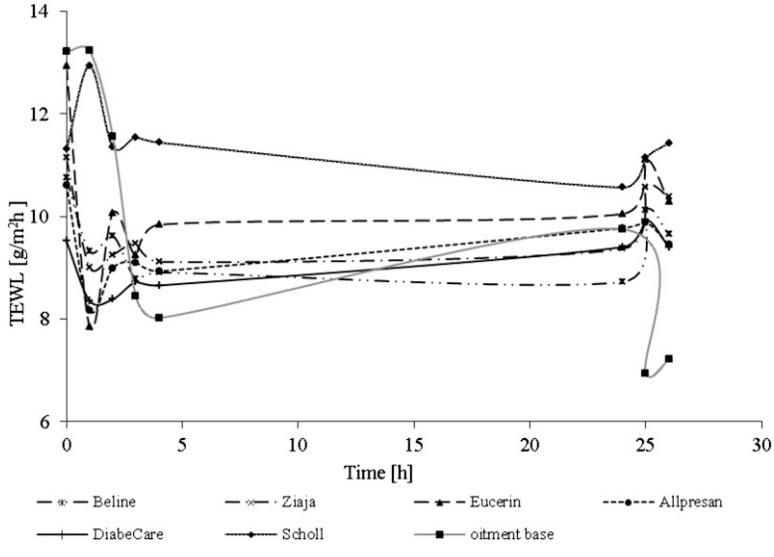


**Figure 4.** TEWL after the application of CP monitored and the ointment base.

**Table II**
TEWL for the Tested CP and the Ointment Base: Mean Value (N = 22)

| | TEWL ($g/m^2/h^{1)}$ | | | | | | | | TEWL ($g/m^2/h^1$) differences vs control | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Time to action of the CP (h) | | | | | | | | | | | | | | | |
| | 0 | 1 | 2 | 3 | 4 | 24 | 25 | 26 | 0 | 1 | 2 | 3 | 4 | 24 | 25 | 26 |
| Control | 15.3 | 11.9 | 12.8 | 10.8* | 13.6* | 12.5 | 13.6* | 11.3* | — | — | — | — | — | — | — | — |
| Beline® | 10.8 | 9.3* | 9.6 | 8.8 | 8.9 | 8.7 | 10.1* | 9.7* | −4.6 | −2.6 | −3.2 | −2.0 | −4.7 | −3.8 | −3.5 | −1.7 |
| Ziaja® | 11.1 | 9.0* | 9.3 | 9.5 | 9.1 | 9.4 | 10.5* | 10.4* | −4.2 | −2.9 | −3.5 | −1.3 | −4.5 | −3.1 | −3.1 | −0.9 |
| Eucerin® | 12.9 | 7.9* | 10.1 | 9.2 | 9.8 | 10.0 | 11.1* | 10.3* | −2.4 | −4.0 | −2.7 | −1.5 | −3.7 | −2.5 | −2.5 | −1.0 |
| Allpresan® | 10.6 | 8.2* | 9.0 | 9.1 | 8.9 | 9.8 | 9.9* | 9.5* | −4.7 | −3.7 | −3.8 | −1.7 | −4.6 | −2.7 | −3.8 | −1.9 |
| DiabeCare® | 9.5 | 8.4* | 8.4 | 8.7 | 8.7 | 9.4 | 9.9* | 9.4* | −5.8 | −3.5 | −4.4 | −2.0 | −4.9 | −3.1 | −3.7 | −1.9 |
| Scholl® | 11.3 | 12.9 | 11.4 | 11.5* | 11.4* | 10.5 | 11.1* | 11.4* | −4.0 | 1.0 | −1.4 | 0.8 | −2.1 | −2.0 | −2.5 | 0.1 |
| Ointment base | 13.2 | 13.2 | 11.6 | 8.4 | 8.0 | 9.8 | 6.9 | 7.2 | −2.1 | 1.3 | −1.2 | −2.3 | −5.6 | −2.8 | −6.7 | −4.1 |

The statistical results of comparisons of test products by measurement times have been presented. *Significance (vs ointment base) $p \leq 0.05$; all other results are non-significant; SD for all the results ranged within limits ± 8.5%.

intervals of hours 1, 25, and 26 ($p < 0.02$) as well as 24 ($p < 0.006$). In contrast, Allpresan® showed significant improvement in hydration ($p < 0.003$) only after 24 h of the application. Regarding support of the protective barrier function of the skin presented through TEWL values, this was confirmed to be significant for Eucerin® after 1 h of application ($p < 0.005$), as well as the 4th and 25th h ($p < 0.001$) of application, whereas for Allpresan®, it was after the 1st ($p < 0.002$), 2nd ($p < 0.001$), 4th ($p < 6.23 \times 10^{-6}$), 24th ($p < 2.36 \times 10^{-8}$), and 25th h ($p < 4.53 \times 10^{-9}$). This suggests that Eucerin® tends to possess moisturizing effects, whereas Allpresan® favors barrier function.

### THE EFFECT OF PERIOD OF CREAM ACTION AND UREA CONTENT ON THE PARAMETERS OF THE SKIN

Contour models were constructed to present the synergistic effect of CP action time (A factor) and urea content (B factor) on the skin parameters monitored (hydration, TEWL).

Figure 5 shows the effect of A factor and B factor on skin hydration. The slope of contour lines in both graphs makes clear that both these factors observed are equally important. For Eucerin® (Fig. 5A), maximum hydration (51.6 c.j.) was measured at the beginning of the test (1 h) with maximum urea content (10%). Hydration gradually decreased over time to approximately 1.0 c.j. after 26 h of exposure to the cream at zero urea content. The model, however, suggests hydration can be increased significantly even after 25 h of exposure to the cream by adding urea; upon 10% addition of urea, hydration increases up to 16.3 c.j. For Allpresan® (Fig. 5B), the maximum value of hydration (23.0 c.j.) occurred at the beginning of the test (1 h) with maximum urea content (10%). Hydration during the first 15 h of action of Allpresan® is approximately twice as low as for Eucerin®, the hydration values being about the same for both CPs after 20 or more hours of action. One should not forget the influence of the foam's urea content on the effect of hydration at the end of the test (hour 25); a 10% addition of urea increases hydration up to about 15.3 c.j. Hydration is affected greatly by glycerol content. The differences between hydration value of both CPs at the beginning of the test, 51.6 c.j. (Eucerin) vs 23 c.j. (Allpresan), can be attributed to a difference in glycerol content in CPs. Relative concentration of urea

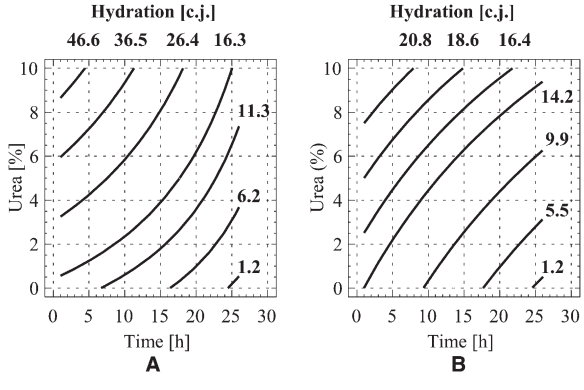


**Figure 5.** Model dependence of skin hydration on CP action time and urea content.
(A) Eucerin®
(B) Allpresan®

and glycerol in the compared CPs is not known. Nevertheless, according to INCI, Eucerin contains (Table I) more glycerol than urea; Allpresan contains less glycerol than urea.

Figure 6 presents a simulation of the influence of A factor and B factor on TEWL. Trends in TEWL development for Eucerin® (Fig. 6A) are equal to those of Allpresan® (Fig. 6B), the difference between the values of the two products being small, whereas that between the minimum and maximum values is approximately twice. At zero urea content and 1 h of action of the products, TEWL is about 13.0 $g/m^2/h$. Lower TEWL values (<10.0 $g/m^2/h^1$) are evident at the addition of more urea (above 6%) and, in fact, are not much affected by the duration of action of the preparations, and at additions of urea less than 6% and with the duration of the creams' action exceeding 15 h. At maximum addition of urea and 1 h of action of the CP, TEWL equals approximately 8.0 $g/m^2/h^1$. The lowest TEWL was recorded for both forms of application at zero addition of urea after 26 h of action of these.

## CONCLUSION

Diabetes affects some functional properties of the epidermis and dermis and may be responsible for a number of skin complaints associated with the disease. Using CPs of proper composition can prevent possible complications like these. Skin care has positive effects on the overall condition of the skin and is one of the fundamental preventative routines of diabetic patients, thereby contributing to the improved quality of their lives. The instrumental techniques used permit, via identification of the selected characteristics of the skin's surface, an appropriate description of the level of hydration effects of the tested commercially available CPs designed for the care of diabetic foot. The level of hydration effect is strongly dependent on the formulation of the product. Even a single application of a CP can induce a temporary regenerative effect in relation to selected characteristics of the skin's surface. Although the observed hydration effect of each CP was similar, comparing the tested CPs (Beline®, Ziaja®, Eucerin®, Allpresan®, DiabeCare®, and Scholl®) containing effective humectants against the ointment base in which any moisturizing substances were absent. This occurred after application of these at monitored time

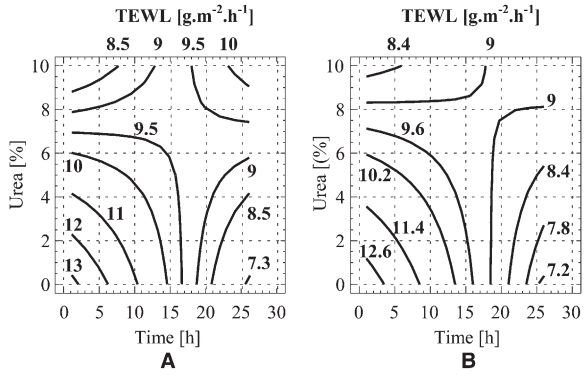


**Figure 6.** Model dependence of TEWL on CP action time and urea content.
(A) Eucerin®
(B) Allpresan®

intervals (1–26 h) using factorial ANOVA evaluation, significant differences were demonstrated. It was confirmed that the ointment base has no significant effect on hydration of the skin. The effect of hydration is thus significantly dependent on the formulation of the product. The same follows from the statistical surveys conducted and dedicated to exploring the differences between Eucerin® and Allpresan®, for which the urea content declared by the producer was 10%. The values of hydration for Eucerin® were higher, by up to half, within the first 2 h immediately after application compared to Allpresan®. It is also obvious that Eucerin® tends to exhibit hydrating effects, whereas Allpresan® favors more barrier properties. A maintained or restored adequate barrier function, as expressed in TEWL, is ensured with urea content above 6% in the CPs, regardless of the duration of their action or lower additions of urea below 4% accompanied by a longer period of CP action.

## ACKNOWLEDGMENT

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