Drug Development and Industrial Pharmacy, 32:239–242, 2006

ISSN: 0363-9045 print / 1520-5762 online
DOI: 10.1080/03639040500466361

Influence of Excipients on Moisturizing Effect of Urea

C. Couteau and
L. J. M. Coiffard
L.P.I.C., Faculty of Pharmacy, SMAB (EA 2160), University of Nantes, 1 rue Gaston Veil, 44035 Nantes Cedex, France

V. Sébille-Rivain
Laboratory of Biomathematics & Biostatistics, Faculty of Pharmacy, University of Nantes, 1 rue Gaston Veil, 44035 Nantes Cedex, France

ABSTRACT Water is the most important molecule contained in the skin and is bound to the intracellular hygroscopic substances called natural moisturizing factors (NMF). The clinical characteristic of xerosis is rough and/or coarse skin. This anaesthetic alteration necessitates cosmetic products application. In this study, we tested the efficiency of urea incorporated into six different emulsions (O/W) and 10 different gels.

Skin of 10 healthy women (20 to 45 years) was treated using 50 mg of emulsion or gel containing 5% of urea. A skin surface of 16 cm^2 was chosen in the area of the forearm. The gain in moisturizing was performed measuring the skin electrical capacity using a corneometer (Courage & Khazaka, model CM 825), one hour after treatment.

Sodium carboxymethyl cellulose gel has the least moisturizing effect. On the other hand, the mixture of polyacrylamide and C13–14 isoparaffin polysorbate 85 can be a good vehicle in the treatment of skin dehydration. Adding various oils (6%) or collagen in aqueous solution does not improve the efficiency of the tested products.

Moisturizing effect of gels (polyacrylamine with C13–14 isoparaffin polysorbate 85) is higher than the one of emulsions (L/H).

KEYWORDS Urea, Moisturizing effect, Gel, Emulsion

INTRODUCTION

Mean water content for an adult varies from 60 to 65% of body weight (40 L), 10% of which is located in the skin, mainly in the dermis and linked to macromolecules, the proteoglycans, and the glycoproteins (Sakai et al., 2000). The epidermis contains about 120 mL of water (60% of its weight) and the corneous layer less than 20 mL (which is 10 to 13% of its weight). Water is settled with the help of hygroscopic substances called natural moisturizing factor (NMF) containing amino-acids (40% including 20 to 30% of serin), pyrrolidoncarboxylic acid (12%), lactic acid (12%), urea (8%), sugars, and minerals (Marty, 2000). A continual transepidermic water flow or insensible water loss increases with lower relative atmospheric humidity and higher temperature. A mean rate of 5 $g.m^{-2}.h^{-1}$ witnesses a healthy skin gate. For an atopic child, the rate varies from 13 to 18 $g.m^{-2}.h^{-1}$. Different dry skin (xerotic) types can be

Address correspondence to C. Couteau, L.P.I.C., Faculty of Pharmacy, SMAB (EA 2160), University of Nantes, 1 rue Gaston Veil, 44035 Nantes Cedex, France; Tel: +(33) 2 40 41 28 73; Fax: +(33) 2 40 41 29 87; E-mail: laurence.coiffard@univ-nantes.fr

observed: the physiological ones (Sakai et al., 2000), the ichtyosiform states, and the ichtyosis (Hanifin, 1991; Akimoto et al., 1993; Kuster et al., 1998). There are numerous origins of xerosis: consequences of sun, dry and cold wind, dry heat exposures, consequences of using unadapted toilet products (soap), or of manipulating some substances.

We will try to classify several moisturizing products, formulated with a true moisturizing agent, urea. We determined, on healthy volunteers, using corneometry, excipient influence on moisturizing effect, by mixing urea into gels (sodium carboxymethylcellulose, acrylates C10-30 alkyl acrylate crosspolymer, . . .), into O/W emulsions and into mixtures of polyacrylamide and C13-14 isoparaffin polysorbate 85.

MATERIALS AND METHODS

Urea, isopropyl myristate, glycerin, and Eutanol G™ were obtained from Cooper (Melun, France). Sodium methyl- and propylparaben and triethanolamin were obtained from Merck, (Fontenay-sous-bois, France). Polyacrylamide, C13-14 isoparaffin ploysorbate 85 (Sepigel™), acrylates C10-30 alkyl acrylate crosspolymer (Carbopol 1342™), cellulose gum (Blanose™), and collagen (Nautigene™) were obtained from Seppic (Castres, France), Goodrich (Brussel, Belgium), Aqualon (Paris, France), and Coletica (Lyon, France), respectively. Distilled water was obtained from an Autostill 400X (Jencons) apparatus.

The formulas realized with or without urea are presented in Tables 1 and 2.

Informal agreement was obtained from 10 healthy women aged 20 to 45 years. These volunteers lay for 20 minutes in a room kept at a constant temperature and relative humidity, respectively 20°C and 50%. A treated skin surface of 16 cm^2 was located on the forearm and delimited by self-adhesive tape (Finn chambers on scanpor, Chiesi, Courbevoie, France). Fifty milligram of product were applied with a glass spatula weighed before and after application. The moisturizing agents were incorporated in oil-in-water (O/W) emulsion, in aquous gel, or in Sepigel™. The gain in moisturizing was performed measuring skin electrical capacity using a corneometer (Courage & Khazaka, model CM 825), at 1 h after treatment on the same volunteers. This method is based on the ability of electrical measurements to predict skin moisturizing states (Loden, 1995).

The statistical analysis was performed using SAS statistical software (SAS Institute, Cary, NC). For continuous variables, the means (SDs) are reported. Gain in moisturizing according to the different formulas was compared using repeated measures ANCOVA with one within-factor (agent), the comparison being adjusted on baseline values. In multiple comparisons, the level of statistical significance was adapted to the number of comparisons according to the Bonferroni's correction.

RESULTS AND DISCUSSION

Urea is known to be a powerful moisturizing agent (Hagstromer et al., 2001; Kuzmina et al., 2002; Gloor et al., 2002) but its efficiency can be modified by the vehicle used.

Concerning the moisturizing effect of each excipient, many differences were observed. As a fact, cellulose gum gel is characterized by its low moisturizing power (Table 3). On the other side, gels obtained with polyacrylamide and C13–14 isoparaffin polysorbate 85 have shown to be very moisturizing itself (Table 3). Whatever oil is used, at a given rate (6%), no significant difference can be noted between the formulas. Below this rate, one can think that the studied oils have no moisturizing effect in a formula (Table 3).

Collagen, introduced at a low concentration, has no effect on the moisturizing power of the gel or emulsion formulated (Table 3).

We obtained the following classification in order of increasing moisturizing power: Gel9 – Gel7 – Gel10 – Emulsion4 – Emulsion1 – Gel1 – Gel4 – Emulsion2 – Emulsion3 – Emulsion6 – Emulsion5 – Gel8 – Gel2 – Gel5 – Gel3.

According to the statistical analysis, cellulose gum gel (without urea) appears to be the least moisturizing formula, followed by a group including some cellulose gum gels with urea and carbomer gel without urea, then a group including basic gel formula using Sepigel™ and emulsion with urea (emulsion 2) and at last, the most moisturizing formula, Sepigel™ with urea (Table 3). The own moisturizing power of Sepigel™ excipient can be interesting as it seems superior to the one of a basic emulsion (without urea) and appears to be a very interesting excipient for some uses in

TABLE 1 **Formulas of Gels Realized**

Ingredients	Gel 1	Gel 2	Gel 3	Gel 4	Gel 5	Gel 6	Gel 7	Gel 8	Gel 9	Gel 10
Sepigel 305	3	3	3	3	3	3				
Carbopol 1342							0.7	0.7		
Blanose									3.5	3.5
Isopropyl myristate	6	6	6							
Eutanol G				6	6	6				
Glycerin	3	3	3	3	3	3	3	3	3	3
Sodium methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Sodium propyl paraben	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Urea		5	5		5	5		5		5
Nautigen			5			5				
Triethanolamine							1	1		
Lactic acid	qs pH 6.5	qs pH 6.5	qs pH 6.5	qs pH 6.5	qs pH 6.5	qs pH 6.5	qs pH 6.5	qs pH 6.5	qs pH 6.5	qs pH 6.5
Distilled water	qsp 100 %	qsp 100 %	qsp 100 %	qsp 100 %	qsp 100 %	qsp 100 %	qsp 100 %	qsp 100 %	qsp 100 %	qsp 100 %

Sepigel 305 = Polyacrylamide, C13–14 isoparaffin polysorbate 85; Carbopol 1342 = Acrylates C10–30 alkyl acrylate crosspolymer; Blanose = Cellulose gum; Nautigene = Collagene.

TABLE 2 **Formulas of Emulsions Realized**

Ingredients	Emulsion 1	Emulsion 2	Emulsion 3	Emulsion 4	Emulsion 5	Emulsion 6
Stearic acid	10	10	10	10	10	10
Coconut oil	7	7	7	7	7	7
Isopropyl myristate	6	6	6	6	6	6
Eutanol G				6	6	6
Glycerin	3	3	3	3	3	3
Sodium methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1
Sodium prpyl paraben	0.05	0.05	0.05	0.05	0.05	0.05
Urea		5	5		5	5
Nautigen			5			5
Triethanolamine	0.3	0.3	0.3	0.3	0.3	0.3
Lactic acid	qs pH 6.5	qs pH 6	qs pH 6	qs pH 6	qs pH 6	qs pH 6
Distilled water	qsp 100	qsp 100	qsp 100	qsp 100	qsp 100	qsp 100

TABLE 3 **Gain in Moisturizing (%) After Application of Various Preparations**

Preparation	Hydration (%) ± SD
Gel 1	83 ± 4
Gel 2	117 ± 6
Gel 3	122 ± 5
Gel 4	82 ± 6
Gel 5	121 ± 5
Gel 6	108 ± 5
Gel 7	63 ± 4
Gel 8	107 ± 6
Gel 9	25 ± 1
Gel 10	69 ± 4
Emulsion 1	77 ± 4
Emulsion 2	89 ± 5
Emulsion 3	92 ± 5
Emulsion 4	73 ± 4
Emulsion 5	99 ± 5
Emulsion 6	94 ± 5

dermatology or in cosmetology due to its high moisturizing power.

REFERENCES

Akimoto, K., Yoshikawa, N., Higaki, Y., Kawashima, M., & Imokawa, G. (1993). *J. Dermatol*, *20*, 1–6.

Gloor, M., Fluhr, J., Lehmann, L., Gehring, W., & Thieroff-Ekerdt, R. (2002). *Skin Pharmacol. Appl. Skin Physiol.*, *15*, 35–43.

Hagstromer, L., Nyren, M., & Emtestan, L. (2001). *Skin Pharmacol. Appl. Skin Physiol*, *14*, 27–33.

Hanifin, J. M. (1991). *Pediatr Clin North Am*, *38*, 763–789.

Kuster, W., Bohnsack, K., Rippke, F., Upmeyer, H. J., Groll, S., & Traupe, H. (1998). *Dermatology*, *196*, 217–222.

Kuzmina, N., Hagstromer, L., & Emtestam, L. (2002). *Skin Pharmacol. Appl. Skin Physiol*, *15*, 166–174.

Loden, M. (1995). *Acta Derm. Venereol. Suppl (Stockh)*, *192*, 1–48.

Marty, J. P. (2002). *Ann Dermatol Venereol*, *129*, 131–136.

Sakai, S., Sasai, S., Endo, Y., Matue, K., Tagami, H., & Inoue, S. (2000). *Skin Res. Technol*, *6*, 128–134.

Sakai, S., Yasuda, R., Sayo, T., Ishikawa, O., & Inoue, S. (2000). *J Invest Dermatol*, *114*, 1184–1187.