International Journal of Cosmetic Science

International Journal of Cosmetic Science, 2010, 1–8 doi: 10.1111/j.1468-2494.2010.00600.x

The moisturizing effect of a wheat extract food supplement on women's skin: a randomized, double-blind placebo-controlled trial

S. Guillou*, S. Ghabri†, C. Jannot†, E. Gaillard‡, I. Lamour‡ and S. Boisnic§,¶

*PROCLAIM, Parc d'affaire de la Bretèche, Bat. B1, 35760 Saint-Grégoire, †Keyrus Biopharma, 53 rue Baudin, 92300 Levallois-Perret, ‡HITEX, Pentaparc, rue Lefèvre-Utile, BP 33601, 56036 Vannes, §GREDECO, Groupe de Recherche et d'Evaluation en Dermatologie et Cosmétologie, 45 Bd Vincent Auriol, 75013 Paris and ¶Dermatologue, service de stomatologie, Hôpital de la Pitié-Salpêtrière, 75013 Paris, France

Received 4 December 2009, Accepted 17 March 2010

Keywords: ceramides, clinical trial, dry skin, food supplement, wheat (*Triticum vulgare*)

Synopsis

Ceramides, specific lipid components of the skin, represent 35–40% of the intercellular cement binding cells together and contributing to skin hydration. A wheat extract rich in ceramides and digalactosyl-diglycerides was developed by Hitex in two forms: wheat extract oil (WEO) and wheat extract powder (WEP). *In vitro* tests and two clinical studies demonstrated promising efficacy results with WEP on skin hydration. To confirm these early results, a double-blind, randomized, placebo-controlled study was carried out on 51 women aged 20–63 years with dry to very dry skin who received either 350 mg of WEO or placebo for 3 months. Evaluation of skin hydration on legs, arms and face, assessed at baseline (D0) and at study end (D84) was performed by the dermatologist using dermatological scores (dryness, roughness, erythema), skin hydration measurement (corneometry) and self-assessment scores (Visual Analogue Scale: VAS). Perceived efficacy was noted by participants throughout the study; tolerability and overall acceptability of the study products were evaluated by the dermatologist and the participants at the end of study. Skin hydration was significantly increased between D0 and D84 on the arms ($P < 0.001$) and legs ($P = 0.012$) in the WEO group compared with placebo. Even if no significant statistical differences between groups were observed for the dermatological evaluation, skin dryness and redness tended to be reduced in the WEO group. Moreover, from D0 to D84, the VAS index had a tendency to increase in favour of WEO for the overall skin hydration ($P = 0.084$) indicating that participants perceived an improvement. The WEO capsules were perceived by participants as being more effective than placebo on all skin dryness signs. In conclusion, WEO capsules were well tolerated and appreciated. After 3 months' treatment, a significant increase in skin hydration and an improvement in associated clinical signs were observed in women with dry skin.

Résumé

Les céramides, principaux lipides composant la peau, représentent 35 à 40% des lipides du ciment inter-cornéocytaire, assurant ainsi la cohésion des cellules et l'hydratation cutanée. Un extrait de blé riche en céramides et digalactosyl-diglycéride, a été développé par Hitex sous deux formes: huile (WEO) et poudre (WEP). Des tests *in vitro* et deux études cliniques sur la forme WEP ont montré des résultats intéressants sur l'hydratation de la peau. Pour les confirmer, une étude randomisée, en double aveugle, versus placebo a été menée chez 51 femmes âgées de 20 à 63 ans présentant une séch-

Correspondence: Emmanuelle Gaillard, HITEX, Pentaparc, rue Lefèvre-Utile, BP 33601, 56036 Vannes, France. Tel.: +33 2 97 68 88 88; fax: +33 2 97 68 88 80; e-mail: egaillard@lavipharm.com

eresse cutanée. Elles devaient ingérer soit 350 mg de WEO soit un placebo pendant trois mois. En début (J0) et en fin d'étude (J84), l'état de la peau des jambes, des bras et du visage a été évalué par un dermatologue à l'aide de scores (sécheresse, rugosité, rougeurs), le degré d'hydratation de la peau a été mesuré (cornéométrie) et une auto-évaluation de la sécheresse cutanée (Echelle Visuelle Analogique) a été réalisée. L'efficacité perçue par les sujets était notée durant l'étude, la tolérance et l'acceptabilité du produit étaient évaluées en fin d'étude par le dermatologue et par les sujets. Le degré d'hydratation de la peau a augmenté significativement entre J0 and J84 sur les bras ($P < 0.001$) et les jambes ($P = 0.012$) dans le groupe WEO. La sécheresse cutanée et les rougeurs ont eu tendance à diminuer dans le groupe WEO, même si aucune différence significative n'a été observée entre les deux groupes. Entre J0 et J84, les femmes ont noté une amélioration globale de l'état d'hydratation de leur peau ($P = 0.084$), et ceci de façon plus marquée dans le groupe WEO. En conclusion, les capsules WEO ont été bien tolérées. Après trois mois de traitement, la sécheresse cutanée et tous ses signes associés ont été améliorés.

Introduction

Dry skin, or xerosis, is a very common problem which is often associated with roughness, squamae, itching, or inflammation and leads to unpleasant sensations and a dull appearance of the skin [1]. Skin is often driest on the arms, lower legs, face, and the sides of the abdomen, but this pattern can vary considerably from person to person. The signs and symptoms of dry skin mostly depend on age, health status and the environment. Moreover, dryness is exacerbated by wind, extreme temperatures, climate-control systems, pollution, chemicals, restrictive diets and sun exposure, among others. These environmental factors and disease states may compromise the barrier function of the *stratum corneum* (SC), leading to excessively dry skin. The SC provides an anti-microbial, anti-oxidant and ultra-violet (UV) radiation barrier. Moreover, the SC plays an integral role in maintaining skin hydration, which is essential for its barrier function [2]. Ceramides, fatty acids and cholesterol are the main lipid constituents of the SC. They are thought to play important roles in water retaining properties and confer the epidermis its barrier property [3–6]. There is an apparent correlation between the composition of skin lipids and skin dryness, and ceramides play a major role in this relationship [7]. Ceramides represent 35–40% of the intercellular cement that binds cells together and contributes to skin hydration. They are mostly endogenous, but a variable amount could be provided by food. It has been shown that dietary sphingolipids are hydrolyzed in the small intestine in bioactive compounds such as ceramides or sphingosines, and then transported through blood flow [8–11]. The composition of the SC changes with age and seasons [12, 13]. Indeed, a decrease in skin lipid concentration has been linked to both winter weather and the ageing process [13, 14], leading to dry skin and all the signs commonly associated, such as squamae, itching, roughness, etc. [15, 16].

Studies have proven that a lack of ceramides in the skin leads to a non-functional hydrolipidic barrier [17], and that topical application of ceramides on dry skin improves skin hydration [18, 19]. Studies on oral lipid supplementation have evaluated the effect of different oils (fish, evening primrose, flaxseed or borage). However, few of these studies have assessed the effect of SC lipids, in particular ceramides, for which the results have been promising. These studies supported the efficiency of ceramides from different plants (konjac, rice, corn) in improving skin hydration [20–22]. All together, these findings indicate that an oral supplementation of ceramides could improve skin hydration.

Until 1997, no botanical ceramides for oral applications were available on the market, only bovine ceramides. In nature, there are a few sources of botanical ceramides: rice, konjac, corn and wheat. Hitex R&D selected non-genetically modified organism (GMO) wheat (*Triticum vulgare*) to develop the first wheat extract rich in ceramides. This botanical lipid extract has a unique composition, rich in polar lipids including sphingolipids such as ceramides and glycosylceramides. It also contains other lipids such as phospholipids, triglycerides and sterols [23, 24]. The non-allergenicity of this wheat extract has been proven and analyses demonstrated the absence of residual gluten. This wheat extract has been developed in two forms, oil (WEO) and powder (WEP). The WEP is obtained by a second extraction on the WEO which corresponds to the triglycerides removal. It has to be noted that the quantity of ceramides and glycosylceramides is similar in 200 mg of WEP and 350 mg of WEO. This wheat extract was

first marketed in 1997 in Japan, pioneer in botanical ceramides research, where it was included in various nutritional supplements and beauty drinks.

Previous *in vitro* tests with human skin explants in culture demonstrated restructuring and hydrating properties, anti-free radicals as well as anti-elastase activity of WEP.

A pilot study was conducted in 2003 in women with normal to dry skin who received either placebo or 80 mg of WEP tablets for 1 month. Results obtained were considered very promising. The WEP tablets tolerance and acceptability were judged excellent throughout the study and the administration of WEP tablets (80 mg daily for 1 month) resulted in a positive trend for an improvement of skin hydration, even in volunteers with normal to moderately dry skin in which it is difficult to observe improvement in skin hydration. However, the duration of 1 month, which represents only one cell renewal cycle, was too short to obtain relevant results.

A second study was conducted in 2005 in women with dry to very dry skin who received either placebo or 200 mg of WEP tablets for 3 months. Results proved that skin hydration, evaluated *via* dermatological scores (squamae, roughness, itching), corneometry and self-assessment, was significantly improved in the WEP group compared with placebo ($P = 0.004$ for leg skin hydration). A significant reduction of the squamae, roughness and itching was also measured in WEP group, which correlates with the increased hydration [25]. These results corroborated those previously obtained in the pilot study as well as the restructuring and hydrating activity of WEP shown *in vitro*.

To confirm these findings, the current clinical study was performed in women with dry to very dry skin to evaluate the moisturizing effect of the WEO (350 mg, four capsules a day for 3 months).

Materials and methods

Study design

This study was a randomized, double blind, placebo controlled clinical trial with two parallel treatment groups: WEO and placebo.

Participants

Fifty healthy women with dry to very dry skin aged between 20 and 63 years completed the study. Participants were recruited in Saint-Grégoire, France (PROCLAIM) *via* a dermatologist after a preliminary interview, a measure of skin hydration on the legs, arms and face and the signature of the informed consent form. The inclusion criteria specified that participants were to be aged between 20 and 65 years, with dry to very dry skin and able to follow the entire study. The evaluation of skin dryness was based on dermatologist's medical examination.

Participants were excluded from the study if they reported any of the following: pregnancy or likely to become pregnant during the study, breastfeeding, history of food allergy, disease, treatment affecting skin hydration or dermatological treatment. The eligible participants received the study products in neutral and coded containers. Subjects were randomized to either WEO (350 mg WEO capsules) or the placebo according to a random list prepared by an independent consulting statistician. The clinical investigator, statistician and subjects remained blinded throughout the trial to avoid bias.

Test products and duration

The lipid extract of non-GMO wheat gluten (*Triticum vulgare*), named Lipowheat™, was developed by Hitex R&D in two forms: oil (WEO) and powder (WEP). In France, these two forms have been authorized as a human food supplement by the DGCCRF (Direction Générale de la Consommation, de la Concurrence et de la Répression des Fraudes). Manufacturing processes and content of residual solvents conform to the European legislation.

The WEO has a unique composition, rich in botanical polar lipids including sphingolipids such as ceramides and glycosylceramides, digalactosyldiglyceride and also other lipids such as phospholipids, triglycerides and sterols. This WEO could be incorporated in various nutritional supplements, beauty drinks, dairy products and biscuits. It is stabilized by a natural preservative derived from rosemary extract and can be stored for 18 months at room temperature with no other special requirements.

The composition of placebo capsules (containing starch instead of WEO) and WEO-based capsules is given in Table I.

The duration of treatment was 12 weeks. Each participant received the food supplement (four

Table I Composition (%) of placebo and wheat extract oil capsules

	Placebo		Wheat extract oil (WEO)	
	Mean weight per capsule (250 mg ± 5%)	Capsules (%)	Mean weight per capsule (270 mg ± 5%)	Capsules (%)
Wheat extract oil	0	0	87	32
Starch	160	64	87	32
Hydrogenated vegetable fat	44	17.5	44	17.5
Fatty acid	44	17.5	44	17.5
Colloidal silicon	2.5	1	2.7	1

capsules a day, two in the morning and two in the evening, corresponding to a daily intake of 350 mg of WEO) or the placebo for 3 months, according to the randomization list. A wash-out period of 1 week, where the application of topical products to the body was avoided, was required before baseline visit (D0) and the end of study (D84).

Study measurements

Hydration measurement: Skin hydration was measured at Day 0 and Day 84 by corneometry (Dermalab®, Cortex, Germany) on legs and arms. Values were expressed as arbitrary units (A.U.). The corneometry measurement principle is based on the bioelectric properties of the skin, which vary with the amount of water in the tissues. Participants were first placed at rest for 15 min in a room with controlled temperature (22 ± 2°C) and humidity (50 ± 10%) with the skin of the arms and calves exposed to the air.

Dermatological evaluation: Skin hydration (dryness, roughness, redness) for the legs, arms and face was assessed at D0 and D84 by the dermatologist using the 5-point Likert scale. A visual examination was performed to evaluate the presence of squamae, dryness and redness by 5 semi-quantitative scores from 0 (none) to 4 (high).

Self-assessment on skin hydration and perceived efficacy: Subjective evaluation of the appearance of the skin on the face and body was noted by participants at D0 and at D84 in a self-assessment diary using a visual analogue scale (VAS) of 10 cm graduated from 'very dry' to 'very hydrated' (one scale for hydration of the face and one scale for hydration of the body).

The perceived efficacy was noted at home by the participants at D14, D28, D42, D56, D70 and at the end of study visit on D84.

Tolerability and acceptability: These criteria were evaluated at the end of study by recording both the adverse events and the overall satisfaction score (out of 10) given by the participant.

Data quality assurance

The investigators performed the study according to ICH-GCP guidelines. Data quality and study monitoring was performed by individuals not in contact with the participants.

Statistical analysis

SAS® (version 9.1, SAS Institute Inc., Cary, North Carolina, U.S.A.) and SPSS® (version 12.0 SPSS Inc., Chicago, IL, U.S.A.) statistical software were used for all statistical analyses. The level of statistical significance was set at $\alpha = 5\%$. No formal sample size calculation was performed. Results were reported as the mean with standard deviation (SD) for continuous variables. Frequency rates were used for the estimation of categorical variables. Differences between the treatment groups were analysed by a two sample *t*-test for continuously distributed variables (or two sample Wilcoxon test if the data did not follow a normal distribution). All efficacy analyses were performed on an intent-to-treat basis.

Results

Participants

The study started in April 2007 and was completed in July 2007. Of 65 women initially screened for eligibility, 51 were included in the study. Data were analysed for 50 women because one participant withdrew from the study for

unrelated reason (house moving). The 50 women were divided into two groups: 25 in the WEO group and 25 in the placebo group. No differences between groups were observed at baseline in demographics: the two groups were comparable with a mean age of 43 ± 11 years (23–59 years) for the WEO group and 42 ± 14 years (20–63 years) for the placebo group. There was also no difference between groups at baseline for skin hydration on the legs, arms and face.

Hydration measurement

Table II shows the inter-group comparison of skin hydration between D0 and D84 for arms, legs and overall (arms and legs). Data showed that WEO significantly increased the degree of skin hydration of the arms ($P < 0.001$), legs ($P = 0.012$) and overall ($P < 0.001$), with the highest increase observed for skin hydration of the arms.

Figure 1 shows the high rate of skin hydration increase (in %) on the arms, legs and overall (legs and arms) after 3 months of WEO consumption. This measure is the mean of individual rates (difference of skin hydration between D84 and D0 divided by the skin hydration value at D0 for each subject). On the arms, WEO has shown a rate of skin hydration increase of 35.1% compared to 0.85% with placebo.

Dermatological evaluation

No skin damage was observed by the dermatologist in the two study groups. Skin dryness and redness for the legs, arms and face tended to be reduced in the WEO group between D0 and D84. However, no statistical differences between groups were observed.

Self-assessment on skin hydration (VAS) and perceived efficacy

Table III summarizes the results of the self-assessment on skin hydration for the face, body and overall (face and body). At D0, VAS index was similar for both groups. Between D0 and D84, the comparison of treatment groups showed a tendency for an increase in skin hydration for both body ($P = 0.080$) and overall ($P = 0.084$) for the WEO group. However, the perception of the facial skin hydration improvement was similar in both treatment groups ($P = 0.174$).

Throughout the study, WEO was perceived by participants as being more effective than placebo on roughness (68% of volunteers vs. 56% for placebo), uniformity of complexion (56% vs. 40%), facial skin hydration (64% vs. 56%), leg skin hydration (52% vs. 36%), suppleness (64% vs. 48%), itchiness (70% vs. 65%) and overall state of the skin (56% vs. 48%) (Fig. 2).

Tolerance and acceptability

No serious adverse events related to the study products were reported. The WEO was well tolerated. Three participants in the WEO group reported either abdominal pain or weight gain or stomach aches and four participants in the placebo group reported either pimples or redness on the face or softer stools or itching on legs. These

Table II Inter-group comparisons of the skin hydration (mean ± SD) from D0 to D84

		Placebo (n = 25)	Wheat extract oil (WEO) (n = 25)	P-value*
Arms	D0	62.25 ± 14.20	63.43 ± 11.71	<0.001
	D84	62.26 ± 17.93	84.25 ± 19.67	
	Δ: D84–D0	+0.01 ± 12.89	+20.83 ± 18.31	
Legs	D0	54.24 ± 17.15	56.04 ± 14.60	0.012
	D84	52.03 ± 12.21	66.69 ± 15.67	
	Δ: D84–D0	−2.21 ± 14.77	+10.65 ± 19.80	
Overall (arms and legs)	D0	58.25 ± 13.12	59.73 ± 11.10	<0.001
	D84	57.02 ± 12.46	75.47 ± 14.44	
	Δ: D84–D0	−1.23 ± 11.23	+15.74 ± 15.47	

n = number of subjects, Δ = difference of mean skin hydration between D84 and D0.
*The statistical test for calculation of P-values was the two sample Wilcoxon test.

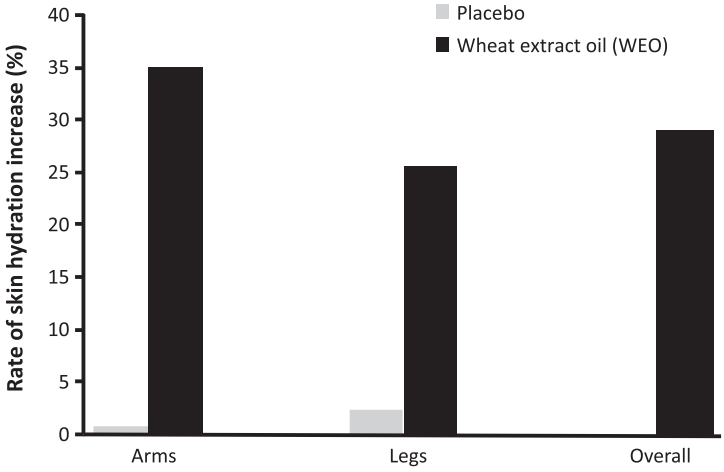

Figure 1 Rate of skin hydration increase (%) on the arms, legs and overall from D0 to D84.

Table III Visual Analogue Scale index (mean ± SD) for self-assessment of skin hydration

		Placebo (n = 25)	Wheat extract oil (WEO) (n = 25)	P-value*
Face	D0	3.12 ± 1.39	2.95 ± 1.76	0.174
	D84	4.89 ± 2.09	5.56 ± 1.71	
	Δ: D84–D0	+1.77 ± 1.97	+2.61 ± 2.08	
Body	D0	1.96 ± 1.05	1.79 ± 1.18	0.080
	D84	3.78 ± 2.38	4.97 ± 2.34	
	Δ: D84–D0	+1.82 ± 2.27	+3.18 ± 2.62	
Overall (face and body)	D0	2.87 ± 1.44	3.38 ± 1.31	0.084
	D84	3.32 ± 1.88	4.17 ± 1.78	
	Δ: D84–D0	+0.46 ± 0.56	+0.79 ± 0.65	

n = number of subjects, Δ = difference of Visual Analogue Scale index between D84 and D0.
*The statistical test for calculation of P-values was the two sample Wilcoxon test.

non-serious adverse events did not cause any withdrawal from the study.

The overall assessment of acceptability was slightly higher for WEO (5.76 ± 2.08) than for placebo (4.84 ± 2.54).

Discussion

This study showed a significant increase in skin hydration on the legs (P = 0.012) and arms (P < 0.001) after 3 months consumption of WEO compared with placebo. However, no statistical differences were obtained between placebo and WEO for the dermatological evaluation by the dermatologist or the participant's self-assessment (VAS). This might be explained by the humidity which was high and unusual during the study. Indeed, it could influence the perception of participants and dermatologist on skin hydration.

These findings are consistent with early results obtained *in vitro*. Indeed, these *in vitro* tests with human skin explants in culture showed restructuring and hydrating properties, anti-free radical activity and anti-elastase activity of WEP [25]. Indeed, (1) the application on broken-down skin cells (acetone-defatted skin) of an emulsion enriched with 1% WEP restructured the skin barrier function; (2) a formulation with 1% WEP led to an anti-free radical activity of approximately 50%; and (3) a 60% inhibition of anti-elastase activity was found with 0.4% of WEP.

A clinical study was conducted in 2005 in 45 women with dry to very dry skin who received either placebo or 200 mg of WEP tablets for 3 months (GREDECO). These women noticed a significant decrease in cutaneous dryness and at the end of study (D90); skin dryness was significantly improved in the WEP group compared with placebo

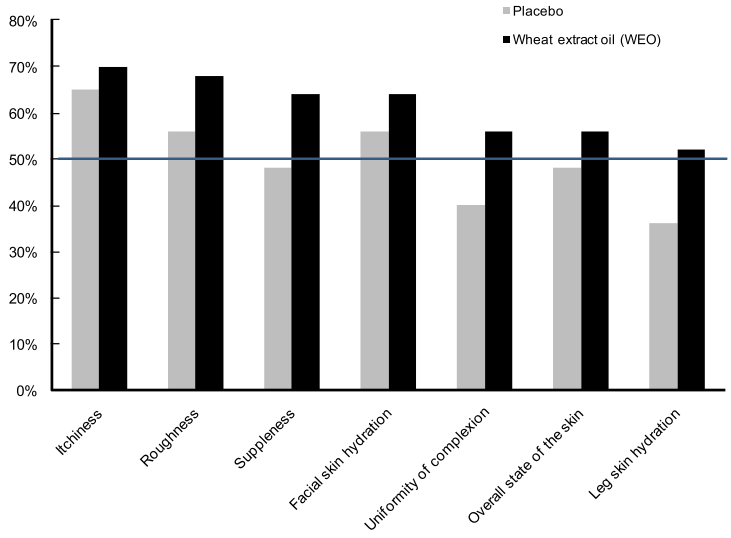

Figure 2 Perceived efficacy by participants at the end of study (D84).

group ($P < 0.05$). Women with considerable itching at D0 noticed a significant decrease at D90 compared with placebo group ($P < 0.01$). The hydration measurements showed that for 95% of the women in the WEP group, there was a significant increase in skin hydration at D90 ($P = 0.01$). A decrease or even a total disappearance of itching was observed for all women who reported considerable itching at D0. At D90, dermatological evaluation indicated a significant decrease in skin squamae for the WEP group compared with the placebo group ($P < 0.01$). These observations indicate that a supplementation of a ceramides-rich ingredient could improve skin dryness. This study brings obvious proofs of ceramides efficacy by oral route.

Even though the quantity of active components (ceramides and glycosylceramides) is similar in 200 mg WEP and 350 mg WEO, improvement of dryness feeling was only significant in the clinical study where women received 200 mg WEP tablets. This might be explained by a different bioavailability of the two different galenic formulations or by the high-humidity during the second study.

Concerning the dose of WEO used in this study (350 mg), it was noticeably weaker than for other nutritional supplement ingredients intended to improve skin hydration [26–28]. Moreover, the daily doses of the other oils have been tested in only a few clinical studies that produced inconsistent results, and except in the case of borage oil, there is no consensus on their efficacy. The WEO dosage at 350 mg has a great advantage for consumers who prefer to limit the number of capsules per day, as well as capsule size. The WEO does not have a sensorial impact on food because the oil is quite neutral and the low dosage keeps it from modifying flavours or odours.

To control the variability of the skin hydration measurements by corneometry and to confirm the WEO efficacy, another method (Moisture Meter SC®; Delfin Technologies Ltd., Kuopio, Finland) could be used for a future clinical study. This method could bring new information and confirm the results obtained with Corneometer and \Dermalab®.

Moreover, to confirm these promising results, a future study could include the analysis of the *stratum corneum* lipid composition (ceramides) after the consumption of WEO.

In conclusion, 350 mg WEO capsules were well tolerated and appreciated. After a 3-month treatment, there is a significant increase in skin hydration and an improvement in associated clinical signs (itching, squamae, roughness, redness, etc.) in women with dry to very dry skin.

Acknowledgements

The authors are grateful to the many research collaborators who have contributed to the article and notably François Laimay and Jean-Philippe Kucma for their constant involvement in wheat extract researches. The authors also thank Kirsten Dumaz of Keyrus Biopharma for proofreading this article. This study was funded by HITEX.

References

1. Barco, D. and Giménez-Arnau, A. Xerosis: a dysfunction of the epidermal barrier. *Actas Dermosifiliogr.* **99**, 671–682 (2008).
2. Jungersted, J.M., Hellgren, L.I., Jemec, G.B. and Agner, T. Lipids and skin barrier function-a clinical perspective. *Contact Derm.* **58**, 255–262 (2008).
3. Holleran, W.M., Man, M.Q., Gao, W.N., Menon, G.K., Elias, P.M. and Feingold, K.R. Sphingolipids are required for mammalian epidermal barrier function. Inhibition of sphingolipid synthesis delays barrier recovery after acute perturbation. *J. Clin. Invest.* **88**, 1338–1345 (1991).
4. Mao-Qiang, M., Elias, P.M. and Feingold, K.R. Fatty acids are required for epidermal permeability barrier function. *J. Clin. Invest.* **92**, 791–798 (1993).
5. Man, M.Q., Feingold, K.R. and Elias, P.M. Exogenous lipids influence permeability barrier recovery in acetone-treated murine skin. *Arch. Dermatol.* **129**, 728–738 (1993).
6. Feingold, K.R., Man, M.Q., Menon, G.K., Cho, S.S., Brown, B.E. and Elias, P.M. Cholesterol synthesis is required for cutaneous barrier function in mice. *J. Clin. Invest.* **86**, 1738–1745 (1990).
7. Stadler, J.F. Hydratation cutanée et atopie. *Ann. Dermatol. Venerol.* **129**, 147–151 (2002).
8. Merrill Jr, A.H., Schmelz, E.M., Wang, E., Dillehay, D.L., Rice, L.G., Meredith, F. and Riley, R.T. Importance of sphingolipids and inhibitors of sphingolipid metabolism as components of animal diets. *J. Nutr.* **127**(5 Suppl.), 830S–833S (1997).
9. Nilsson, A. and Duan, R.D. Absorption and lipoprotein transport of sphingomyelin. *J. Lipid Res.* **47**, 154–171 (2006).
10. Sugawara, T., Kinoshita, M., Ohnishi, M., Nagata, J. and Saito, M. Digestion of maize sphingolipids in rats and uptake of sphingadienine by Caco-2 cells. *J. Nutr.* **133**, 2777–2782 (2003).
11. Vesper, H., Schmelz, E.M., Nikolova-Karakashian, M.N., Dillehay, D.L., Lynch, D.V. and Merrill Jr, A.H. Sphingolipids in food and the emerging importance of sphingolipids to nutrition. *J. Nutr.* **129**, 1239–1250 (1999).
12. Saint Léger, D., François, A.M., Lévêque, J.L., Stoudemayer, T.J., Grove, G.L. and Kligman, A.M. Age-associated changes in stratum corneum lipids and their relation to dryness. *Dermatologica* **177**, 159–164 (1988).
13. Rogers, J., Harding, C., Mayo, A., Banks, J. and Rawlings, A. Stratum corneum lipids: the effect of ageing and the seasons. *Arch. Dermatol. Res.* **288**, 765–770 (1996).
14. Grove, G.L. and Kligman, A.M. Age-associated changes in human epidermal cell renewal. *J. Gerontol.* **38**, 137–142 (1983).
15. Denda, M., Koyama, J., Hori, J., Horii, I., Takahashi, M., Hara, M. and Tagami, H. Age- and sex dependent change in stratum corneum sphingolipids. *Arch. Dermatol. Res.* **85**, 415–417 (1993).
16. Hashizume, H. Skin aging and dry skin. *J. Dermatol.* **31**, 603–609 (2004).
17. Rawlings, A.V. Trends in stratum corneum research and the management of dry skin conditions. *Int. J. Cosmet. Sci.* **25**, 63–95 (2003).
18. Imokawa, G., Akasaki, S., Minematsu, Y. and Kawai, M. Importance of intercellular lipids in water-retention properties of the stratum corneum: induction and recovery study of surfactant dry skin. *Arch. Dermatol. Res.* **281**, 45–51 (1989).
19. Yilmaz, E. and Borchert, H.H. Effect of lipid-containing, positively charged nanoemulsions on skin hydration, elasticity and erythema – an *in vivo* study. *Int. J. Pharm.* **307**, 232–238 (2006).
20. Primavera, G. and Berardesca, E. Clinical and instrumental evaluation of a food supplement in improving skin hydration. *Int. J. Cosmet. Sci.* **27**, 199–204 (2005).
21. Asai, S. and Miyachi, H. Evaluation of skin-moisturizing effects of oral or percutaneous use of plant ceramides. *Rinsho Byori* **55**, 209–215 (2007).
22. Kimata, H. Improvement of atopic dermatitis and reduction of skin allergic responses by oral intake of konjac ceramide. *Pediatr. Dermatol.* **23**, 386–389 (2006).
23. Deschamps, F.S., Gaudin, K., Baillet, A. and Chaminade, P. Wheat digalactosyldiacylglycerol molecular species profiling using porous graphitic carbon stationary phase. *J. Sep. Sci.* **27**, 1313–1322 (2004).
24. Sugawara, T. and Miyazawa, T. Beneficial effect of dietary wheat glycolipids on cecum short-chain fatty acid and secondary bile acid profiles in mice. *J. Nutr. Sci. Vitaminol (Tokyo)* **47**, 299–305 (2001).
25. Boisnic, S. and Branchet, M.C. Intérêt clinique d'un ingrédient alimentaire à visée hydratante: Lipowheat™. Etude randomisée en double aveugle versus placebo. *J. Méd. Esth. Et Chir. Derm.* Vol. XXXIV, **136**, 239–242 (2007).
26. Henz, B.M. Double blind, multicentre analysis of the efficacy of borage oil in patients with atopic eczema. *Br. J. Dermatol.* **140**, 685–688 (1999).
27. Morse, P.F. Meta-analysis of placebo-controlled studies of the efficacy of Epogam in the treatment of atopic eczema. Relationship between plasma essential fatty acid changes and clinical response. *Br. J. Dermatol.* **121**, 75–90 (1989).
28. Whitaker, D.K. Evening primrose oil (Epogam) treatment of chronic hand dermatitis: disappointing therapeutic results. *Dermatology* **193**, 115–120 (1996).