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ORIGINAL RESEARCH

Cichorium intybus root extract: A "vitamin D-like" active ingredient to improve skin barrier function

P. M. B. G. Maia Campos[a], D. G. Mercurio[a], M. O. Melo[a] and B. Closs-Gonthier[b]

[a]NEATEC, Faculty of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirao Preto, Brazil; [b]R&D Department, SILAB, Brive Cedex, France

ABSTRACT

During the aging process, the human skin suffers many alterations including dryness, skin barrier function damage. The skin barrier function is important to the prevention of skin alterations and maintenance of homeostasis. So, the objective of this study was to assess the clinical efficacy on skin barrier function of *Cichorium intybus* root extract in cosmetic formulations with or without UV filters. Fifty women, aged between 45 and 60 years, were divided into two groups. One group received vehicle formulations containing UV filters, and the other group received formulations without UV filters. Both groups received a formulation containing the extract and the vehicle. The formulations were applied twice daily to the upper arms after washing with sodium lauryl sulphate. Transepidermal water loss (TEWL) and skin microrelief were evaluated before and after a 14- and 28-day period of treatment. The control regions and regions where the vehicles were applied showed an increase in the TEWL. For the formulations containing the extract, decreased TEWL and improved microrelief were observed when compared to the vehicle and control areas after a 28-day period. In conclusion, *Cichorium intybus* root extract showed protective and restructuring effects on the skin and stands out as an innovative ingredient to improve skin barrier function.

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KEYWORDS
TEWL; skin barrier function; chicory extract; vitamin D like; clinical study; photoprotective formulations

Introduction

During the aging process, the human skin suffers many alterations including dryness, skin barrier function damage and others that could lead to an increase in skin sensibility (1).

The use of cosmetic products to improve skin protection, mainly from damages caused by UV radiation, and skin barrier function maintenance is essential for keeping the skin in good condition. Considering the benefits in the topical use of vitamins (2–4), the search for new active ingredients that have similar effects is fundamental to the development of stable and safe cosmetic formulations, as most part of vitamins are unstable when added to topical formulations (5–7). This way, the use of natural extracts with vitamin-like properties, that are more stable and skin compatible, are an important alternative to obtain effective topical formulations to skin protection.

According to *in vitro* studies, the chicory root extract increases the number of vitamin D receptors (VDR) by stimulating their synthesis due to its rich composition in oligofructosans (8). When stimulated by vitamin D, the receptor ligand complex binds to vitamin D response elements, which are specific DNA sequences in the nucleus that affect the transcription of target genes that regulate cellular proliferation and differentiation (9,10). It can be integrated into skin care products for mature skin, as it enables the mature skin to recover epidermal barrier health without sun exposure.

In this context, the development of cosmetic formulations containing chicory root extract, as well as its clinical efficacy evaluation, is very important to obtain effective products to improve skin protection.

Thus, the objective of this study was to evaluate the short-term clinical efficacy on skin barrier function improvement of *Cichorium intybus* (chicory) root extract vehiculated at 3% in cosmetic formulations with or without UV filters.

Materials and methods

For this study, two formulations were developed, one as a gel cream (F1 and F2) and the second based in an UV filter formulation (F3 and F4), both with and without 3% of *Cichorium intybus* root extract (Silab, Brive, France), respectively.

The gel cream formulation was based on Sodium Polyacrylate, Dimethicone, Cyclopentasiloxane, Trideceth-6, PEG/PPG-18/18 Dimethicone, Acrylates/C10–30 Alkyl Acrylate Crosspolymer. The UV filters of the second formulation were bis-ethylhexyloxyphenol methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate, ethylhexyl triazone, ethylhexyl methoxycinnamate and titanium dioxide.

After approval from the ethics committee (CEP/FCFRP 143/2008), a group of 50 healthy female volunteers between 45 and 60 years old were recruited to participate in the clinical efficacy study, with 25 women using the formulation with UV filters and 25 without UV filters. The volunteers received both the vehicle and the formulation with chicory root extract, and the formulations were randomly applied twice a day on the upper arm area for 28 days. Additionally, the volunteers were guided to wash the whole arm skin area with a 10% sodium lauryl sulphate solution before applying any formulations and to designate an area as a control region (without the application of any formulation) on both arms.

CONTACT P. M. B. G. Maia Campos pmcampos@usp.br Faculty of Pharmaceutical Science of Ribeirão Preto, University of São Paulo, Avenida do Café, s/n, CEP 14040-903, Ribeirão Preto, SP, Brazil

Measurements were made on three areas for both groups, the non-treated control area, the vehicle area and the product area (with or without sun protection). The measurements of transepidermal water loss (TEWL) were made with a TM 210 Tewameter® (Courage & Khazaka, Germany), which provides information on the quality of the barrier function of the *stratum corneum*. This instrument measures the percentage of relative humidity at the skin surface and is based on the principles described by Adolf Fick in 1885. The values are registered in g/m^{2}h (11).

The image-digitalization process was accomplished using Visioscan® VC 98 (Courage & Khazaka, Germany), which is a unique UVA-light video camera with high resolution to study the skin surface directly. The camera features a high resolution black and white video sensor and a ring shaped UV-A light source (which presents no hazard to normal human skin) for uniform illumination of the skin (12).

Results

Transepidermal water loss

The group without sun protection (Group 1) and the control areas showed a significant increase in TEWL after 14 and 28 days of the study. This effect was also observed in the region treated with the received formulation without the active ingredient under study. The region receiving the formulation containing 3% of chicory root extract did not present significant differences between D0 and D28. The formulations containing the active ingredient protected the skin barrier function from increased water loss provoked after SLS application (Figure 1). In addition, the region treated with the formulation containing 3% chicory root extract (F2) presented significantly different values of TEWL from the region when compared to the region receiving the vehicle formulation (F1) at D28 (Figure 1). Regarding the group receiving sun protection (Group 2), the F4 control area showed a significant increase in TEWL after 14 and 28 days of the study. In contrast, in the region where formulations F2 and F4 were applied, a reduction of the TEWL values was observed, but this reduction was significant only for the F4 formulation. Thus, the formulation with chicory root extract and UV filters showed more pronounced effects on the protection of the skin barrier function after SLS application when compared with the formulation containing only the extract under study.

No significant differences were observed between the effects of the F2 and F4 formulations 28 days. Thus, both formulations were effective for skin protection. Formulation F4 showed significant differences from formulations F1 and F3. In addition, the formulation containing UV filters and *Cichorium intybus* root extract (F4) presented significantly different values of TEWL from the control region at D28. This way, the skin protective effects of this formulation were more pronounced.

The region that received the formulation containing 3% of chicory root extract with sun protection SPF25 (F4) presented TEWL significantly different from the region receiving F1 and F3 at D28. A significant difference was not observed between the effects of formulations F2 and F4 with *Cichorium intybus* root extract after 28 days of use (Figure 2).

Skin microrelief analysis

According to skin microrelief images analysis, the control areas showed an increase in skin roughness, scaliness and increased depth of the furrows after 28 days of study, an effect from the SLS application as it damages the skin (Figure 3(A) and (B)). In the region where the gel cream formulation (F1) was applied, we observed an increase in skin scaliness, a loss of the rhomboidal pattern and an increase of skin roughness, as the formulation did not protect from SLS damage (Figure 3(C) and (D)). As the region receiving the formulation UV filters (F3) did not show differences in skin microrelief when compared to baselines values, this

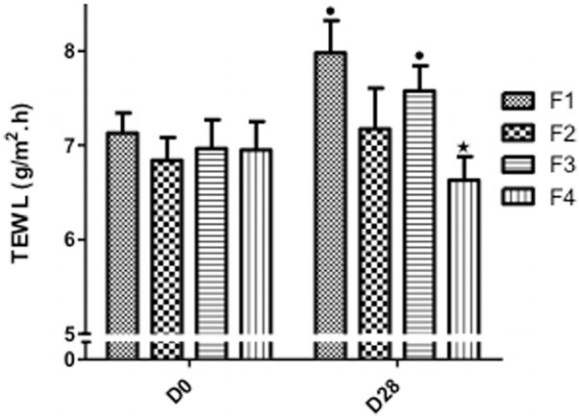

Figure 2. Transepidermal water loss before (D0), and after 28 days (D28) of application of the gel cream vehicle and containing the active ingredient under study (formulations F1 and F2, respectively) and UV-filter vehicle and with 3% of *Chichorium intybus* root extract (formulations F3 and F4, respectively) (Wilkoxon rank signed test, $n = 26$, mean ± SEM). •Significantly different from baseline (D0) values: $p < 0.05$. ★Significantly different from F1 and F3 at D28: *$p < 0.05$.

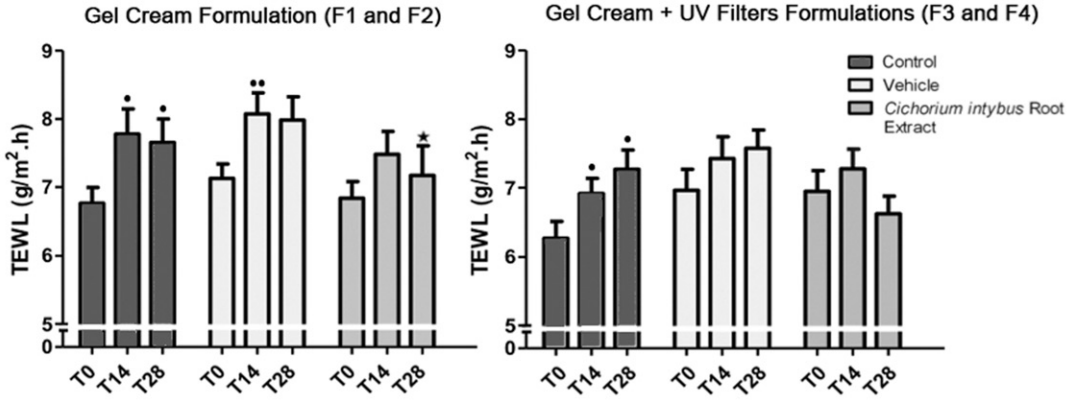

Figure 1. Transepidermal water loss before (D0), and after 14 and 28 days (D14 and D28) of application of the formulations F1 and F3 (vehicle) without or with 3% of *Chichorium intybus* root extract (F2 and F4) and their respective control areas (Wilkoxon rank signed test, $n = 26$, mean ± SEM). •Significantly different from the baseline values: •$p < 0.05$; ••$p < 0.01$. ★Significantly different from vehicle after 28 days: $p < 0.05$.

treatment had protective effects ondamage from SLS (Figure 3(G) and (H)). For the formulations of gel cream and gel cream with UV filters containing the studied active ingredient (F2 and F4), the skin microrelief profile improved with a reduction of skin roughness, improvement of skin rhomboidal pattern and reduction of the depth of the furrows when compared to control region showing the beneficial effects of the formulations with *Cichorium intybus* root extract on skin recovery (Figure 3(E), (F), (I) and (J)).

In the quantitative micro relief analyzes, the control region had a significant increase of skin roughness after 28 days of study due to the skin damages caused by the SLS application while the regions where the formulations F1 and F2 where applied the skin roughness did not suffer any significant alterations. In addition, the regions where formulations F3 and F4 were applied acted reducing these values, showing a protective effect. However, this effect was not significant (Figure 4).

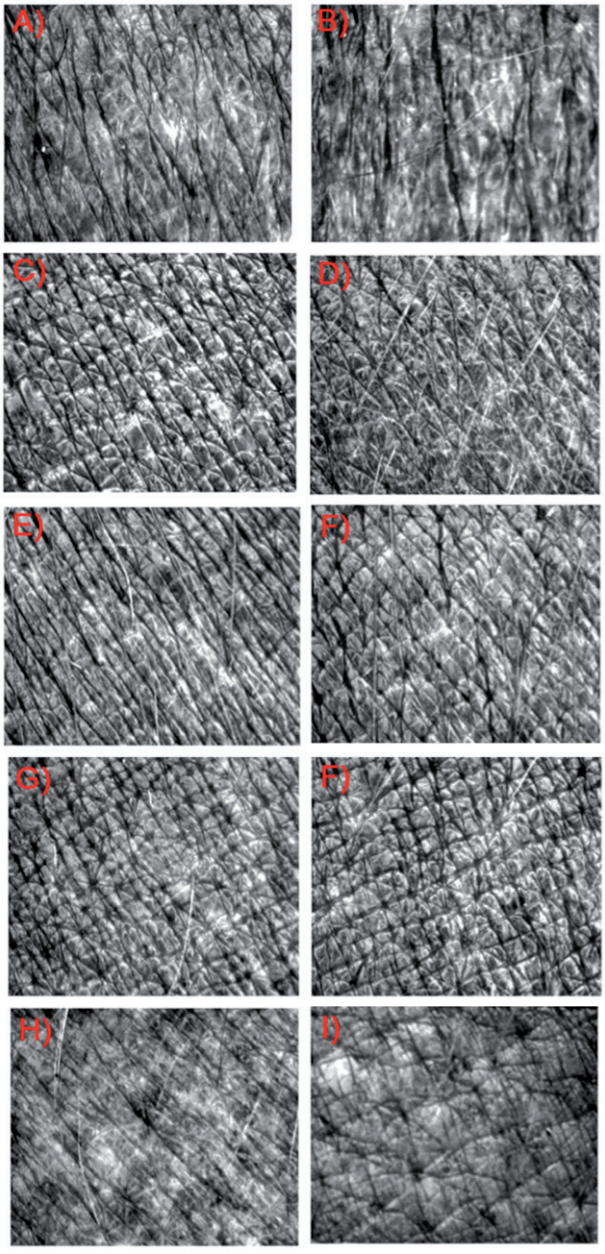

Figure 3. Skin microrelief images. Microrelief of a volunteer's control area before and after (A and B) a 28-day period of use of SLS. Images (C) and (D) represent a skin microrelief before and after the use of the gel cream (F1). Images (E) and (F) represent a skin microrelief before and after the use of the gel cream +3% of *Chichorium intybus* root extract (F2). Images (G) and (H) represent a skin microrelief before and after the use of the gel cream + UV filters formulation (F3). Images (E) and (F) represent a skin microrelief before and after the use of the gel cream UV filters +3% of *Chichorium intybus* root extract (F4).

Discussion

The concept of vitamin-like ingredients has been emerging as promising active ingredients to be used in topical formulations to recover skin barrier function and keep skin homeostasis.

In this study, the formulations containing chicory root extract showed *in vivo* protective effects on the skin where SLS was applied. Application of SLS on the skin can modify the composition of the lipid components in the epidermis and cause disruption of the multiple lamellae structures (13–15). The use of a solution containing SLS after 2 and 4 weeks caused a progressive increase on TEWL. This increase was also observed on the regions where the placebo formulations were applied. The results also showed clinical effects of the active ingredient under study on the improvement of skin barrier function, while the region where formulations with chicory root extract were applied did not increase TEWL after a 28-day period.

The obtained clinical effects can be due to the rich composition in oligofructosans of the studied extract acting in the hydrolipidic mantle, regenerating the skin barrier and leading to a reduction of the TEWL. In addition, the results could be related to the recovery of the functions of the VDR such as stimulating the molecular network involved in the terminal differentiation of keratinocytes (16), accelerating the recuperation of the barrier function and having a restructuring effect.

Beyond skin barrier function, the effects observed in skin microrelief also revealed the restructuring effects of the chicory root extract. According to the obtained micro relief images the impairment of skin microrelief caused by SLS application (control regions) was not recovered by formulations without the active ingredient. However, the formulations containing the active ingredient under study was able to not only prevent skin roughing but also improve the skin microrelief after the period of the study. Moreover, the improvement on skin micro relief could be related to skin hydration.

Improvement of skin barrier function is a subject of major interest within dermatological and cosmetic areas. The use of moisturizing formulations improves the skin barrier function by their rich composition acting on the balance of the hydrolipidic mantle of the skin (15,17). Beyond the moisturizing effects, chicory root extract acts on the increase of the number of VDR *in vitro* studies (18). Thus, *Cichorium intybus* extract is a useful ingredient to be applied in cosmetic products to prevent dry skin alterations and

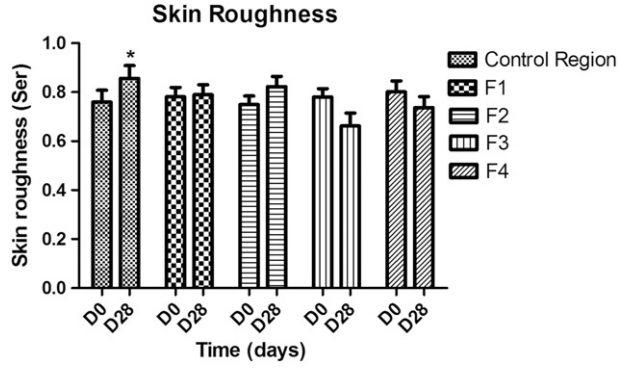

Figure 4. Skin roughness (Ser) before (D0) and after 28 days (D28) of the application of the formulations F1, F2, F3, F4 and control region (Wilkoxon rank signed test, $n = 26$, mean ± SEM).

topical formulations for skin diseases such as atopic dermatitis and acts on an additional mechanism for the improvement of skin barrier function, maintaining physiological skin conditions, since TEWL may impact skin healthy and lead to skin disorders.

Concerning UV photo-protection, the use of sunscreen has a negative impact on vitamin D production (17,19), which can impair the physiological balance of skin proliferation and differentiation in the epidermis. Furthermore, the VDR signalling pathway plays an important role in cancer prevention by contributing to cellular responses to UVB radiation–induced DNA damage (20–24). This way, a sunscreen containing chicory root extract presents additional benefits for UV damage prevention.

Thus, to keep the integrity of the skin barrier and to enhance protection against UV-induced DNA damage, the combination of vitamin D-like and UV filters is very promising. The vitamin D-like action compensates for the deleterious effects of the reduction of vitamin D in the cutaneous tissue and can promote excellent protective and restructuring effects.

In conclusion, *Cichorium intybus* (chicory) root extract showed protective and restructuring effects on the skin, acted to reduce the TEWL and improved skin microrelief. In addition, the association of UV filters and chicory extract presents complementary benefits by providing skin barrier and UV protection. This way, *Cichorium intybus* (chicory) root extract stands out as a useful active ingredient to improve skin barrier function, maintaining physiological skin conditions, since TEWL may impact in skin health.

Disclosure statement

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