Cistus ladanifer based hand cream for chilblains

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Abstract

Background: Chilblains are caused by inflammation of small blood vessels in response to exposure to cold temperatures. This condition causes symptoms such as itching, red patches, localized swelling and pain. Emollients are used to protect this skin but are often considered uncomfortable. Most consumers prefer a spray product, with a non-greasy feel. This study aims to develop a hand cream to circumvent existent limitations and comply with consumers' sustainability preferences.

Methods: The prototypes were designed through an overall eco-friendly approach. The key ingredient was *Cistus ladanifer* hydrolate, based on traditional use. Texture, skinfeel and appearance were defined as critical parameters. The selected prototype was further tested through Challenge Test (ISO 11930:209) and submitted to stress conditions (4 weeks, alternating 5ºC and 40ºC storage each 24h) for preliminary assessment of stability.

Results: Several prototypes were designed to be cold processable and were prepared using moisturizing and restorative ingredients. An eco-friendly glass flask with a metallic roll-on applicator was selected. This provides easy spreading, a refreshing sensation and yields a massage upon application. The selected composition is protected against microbial contamination (criteria A, challenge test) and was stable under stress conditions.

Conclusions: The product developed addresses consumer's preferences and combines eco-friendly properties, tradition by using an autochthonous natural ingredient with key functional properties, comfort upon application and a particular ingredient combination designed to provide relief and preserve skins' integrity.

Keywords: Chilblains, Cistus ladanifer hydrolate, natural product, sustainable cosmetic

Introduction. Chilblains are caused by small blood vessels inflammation that occur in response to repeated exposure to cold temperatures. This condition causes great discomfort and symptoms include itching, red patches, localized swelling and pain [1,2,3]. It is prevalent in all age groups but occurs most commonly in young adults and particularly among women [4]. In previous studies we unraveled consumer's perceptions on chilblains non-pharmacologic approaches and found that commercially available products are considered uncomfortable, leaving an oily residue and interfering with normal daily activities. Only about half of the 336 volunteers believed that the products they used improved their quality of life. Regarding an idealized product, most consumers preferred a spray product, with a non-greasy skin feel (33%) over a gel form (22%), a solution to be dried afterwards (11%), a cream(11%) or an ointment (3%) [5].

A clear trend for sustainable cosmetic products is currently perceived, including a broad range of eco-friendly and natural concepts. Consumers are increasingly searching for "green" cosmetic products, and plant extracts have gained importance as natural alternatives.

Cistus ladanifer is a plant belonging to the *Cistaceae* family that naturally occurs in Portugal forests and has traditionally been used for cosmetic purposes, particularly for perfumes. This shrub species is known for conditioning, anti-inflammatory and antisseptic properties [6].

Essential oils are obtained by hydrodistillation or steam distillation of plant parts, such as leaves, branches, stems and roots [6, 7]. During this process, not only the essential oil is obtained but also the hydrolate which has hydrophilic properties [8, 9]. The essential oils of *Cistus ladanifer* are the most studied of all extracts due to their intrinsic bioactivities [8]. Previous studies have demonstrated that these extracts show antimicrobial activity against Gram positive bacteria (*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Bacillus subtilis*, *Bacillus megaterium*), Gram negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*), yeasts and fungi (*Aspergillus niger*, *Botrytiserea spp.*, *Mucor racemosus*) [8]. *C. ladanifer* essential oils are mainly composed of terpenoid compounds, mostly mono and

sesquiterpenes, which have been previously associated with a high antimicrobial activity [10]. Aqueous extracts, in turn, have high amounts of polyphenolic and flavonoid compounds and a stronger antimicrobial activity against *S. aureus* (Gram-positive) than to *E. coli* (Gram-negative) [11]. Studies carried out on both essential oils and other types of *C. ladanifer* extracts, namely aqueous, ethanolic, methanolic and hydroacetanolic bioextracts, show that the phenolic and flavonoid compounds present in these extracts, are associated with a powerful antioxidant activity [8, 12].

The aim of the study was to develop an innovative product specifically designed towards consumer's needs and preferences. The product developed should be moisturizing and emollient, provide a refreshing feeling after application and do not leave an oily sensation on the skin**.** Sustainability claims should be evident for this product.

Materials and Methods. The prototypes were rationally developed based on an eco-friendly approach from ingredient selection, through production methods and packaging selection. The key ingredient was defined as *Cistus ladanifer* hydrolate based on its traditional use for wound healing. The extract was acquired to local producers in Portugal to further support a low environmental impact strategy for the product. A fluid texture (lotion), intended to be applied as a spray or roll-on was selected as the target presentation for this project. Texture, skin-feel and appearance were defined as critical parameters for the product.

The selected prototype was further tested through Challenge Test (ISO 11930:2019).This standard describes the method for testing the preservatives efficacy in cosmetic formulations that are not considered low risk according to international standard ISO 29621. Briefly, the preservative efficacy of the formulation was evaluated by inoculating the formulation with a calibrated suspension of microorganisms defined as relevant in the standard (*S. aureus* ATCC 6538, *P. aeruginosa* ATCC 9027, *E. coli* ATCC 8739, *C. albicans* ATCC 10231 and *A. brasiliensis* ATCC 16404). The number of viable microorganisms was determined at defined intervals over a 28-day assay (7, 14, and 28 days). At each time, the logarithmic reduction was calculated and compared to the minimum requirements defined in the standard for product classification based on two criteria: A and B. Criteria A classifies the products that presented the most pronounced logarithmic reduction profile over time, and criteria B

includes the products that present an acceptable microbial load reduction profile. Additional measures must be taken to prevent microbial proliferation for products in the last criteria.
The selected prototype was submitted to storage temperature stress conditions during 4 weeks, by alternating 5ºC and 40ºC storage each 24h, for preliminary assessment of stability.

Results. Several prototypes were designed through the rationale defined for the product using the locally sourced *Cistus ladanifer* hydrolate combined with a vitis vinifera oil also produced in Portugal and other moisturizing and restorative ingredients. Fragrance was not added to the formula to avoid irritant and sensitizing effects. Fluid textures as gels and emulsions were formulated and based on the sensorial properties of these prototypes we perceived that emulsions would provide more comfort during application than gels would (Table 1).

Table 1 – Prototypes developed according to the defined Product Target Profile and their sensorial evaluation and further approval status

Prototype version	INCI List	Sensory evaluation	Approved or rejected
A	Aqua, xanthan gum, gellan gum, panthenol, chamomilla recutita flower extract, cistus ladanifer leaf extract, glycerin, phenoxyethanol, benzoic acid, dehydroacetic acid, sodium citrate	-Non confortable skin feel after application - difficult to dry; -Lumpy Formulation;	Rejected
B	Aqua, xanthan gum, panthenol, chamomilla recutita flower extract, cistus ladanifer leaf extract, glycerin, phenoxyethanol, benzoic acid, dehydroacetic acid	-Non confortable skin feel after application - difficult to dry;	Rejected
C	Aqua, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, panthenol, chamomilla recutita flower extract, cistus ladanifer leaf extract, glycerin, vitis vinifera seed (grapeseed) oil, caprylic/capric triglyceride, phenoxyethanol, benzoic acid, dehydroacetic acid	-Confortable skin feel after application; -Sprayable characteristic needs to be improved; -Unstable emulsion;	Rejected
D	Aqua, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, lauryl glucoside, myristyl glucoside, polyglyceryl-6 laurate, panthenol, chamomilla recutita flower extract, cistus ladanifer leaf extract, glycerin, vitis vinifera seed (grapeseed) oil, caprylic/capric triglyceride, phenoxyethanol, benzoic acid, dehydroacetic acid	-Confortable skin feel after application -Sprayable and roll on compatible formula	Approved

E	Aqua, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, lauryl glucoside, myristyl glucoside, polyglyceryl-6 laurate, panthenol, cistus ladanifer leaf extract, glycerin, vitis vinifera seed (grapeseed) oil, caprylic/capric triglyceride, phenoxyethanol, benzoic acid, dehydroacetic acid	-Confortable skin feel after application -Sprayable and roll on compatible formula	Approved

Prototype E was selected to proceed for further characterization. This formula was designed to be cold processable, allowing for an energy-saving industrial production process.

For packaging, an eco-friendly glass flask with a metallic roll-on applicator was selected. This packaging provides easy spreadability, a refreshing sensation and yields a massage of the skin without the use of hands. Besides the comfort provided by this application, it also represents an added value of the product as it activates microcirculation near the sensitive area. The chosen packaging also has the advantage of reducing the risk of microbiological contamination from application by sparing the use of hands when applying the product and reducing the contact of the packed product with air.

The selected composition is protected against microbial contamination according to the Challenge Test results (Table 2 and Figure 1) showing a microbial load reduction profile compatible with Criteria A.

Table 2 – Colony forming units (CFU) counts and log reduction regarding the initial inoculum (Δlog) in Challenge Test; w/I - without increasing in the CFU number; I – increased number of CFU; NA – not according to standard requirements.

Microorganisms	7 days (CFU)	7 days (Δlog)	14 days (CFU)	14 days (Δlog)	28 days (CFU)	28 days (Δlog)	Criterion
S. aureus ATCC 6538	1.00E+01	5.25	1.00E+01	5.25 (s/A)	1.00E+01	5.25 (s/A)	A
P. aeruginosa ATCC 9027	1.00E+01	4.92	1.00E+01	4.92 (s/A)	1.00E+01	4.92 (s/A)	A
E. coli ATCC 8739	1.00E+01	5.16	1.00E+01	5.16 (s/A)	1.00E+01	5.16 (s/A)	A
C. albicans ATCC 10231	1.00E+01	4.38	1.00E+01	4.38 (s/A)	1.00E+01	4.38 (s/A)	A
A. brasiliensis ATCC 16404	---	---	1.00E+01	3.75	1.00E+01	3.75 (s/A)	A

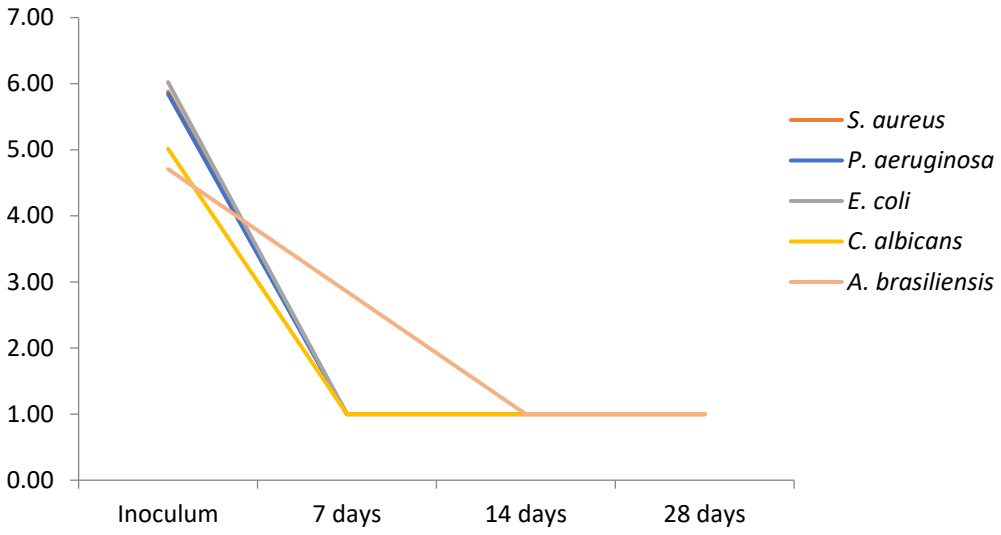

Figure 1 - CFU log values of the five microorganisms included in the test for the initial inoculum (concentration in the sample) and for the sample during the Challenge Test study.

No significant changes in sensorial properties were observed after the stress conditions cycles. Stability for, at least, 2 months at room temperature (real time stability) was also confirmed for all tested parameters (sensorial properties, pH, viscosity and microbial quality).

Discussion

This hand cream, with very fluid texture, was developed under a strong rational of consumers preferences and needs regarding chilblains and skin care. All ingredients were selected based on safety parameters and considering sustainability parameters.

Consumers with frequent chilblains experience the need for frequent use of hand cream and complain about discomfort and limitations of the marketed products. While, in some cases, there is the need to apply drug products (such as corticosteroids) to manage this condition [18], the use of cosmetics as a first line routine care of these skin areas is important to promote the skin barrier and avoid lesions. Gathering cosmetic efficacy and acceptability properties is, therefore, essential for consistent use of these products. In this case, formula development

was also driven by safety concerns related to sensitive skin and impaired barrier function of this condition. This is the main reason why fragrance was avoided as an ingredient of this hand cream.

Besides sensorial properties and cosmetic efficacy and safety, cosmetics are chosen based on lifestyle preferences. Sustainability and natural compositions are influencing the choices of current consumers, especially the young active consumers [14,15]. Other aspects such as culture and tradition (including traditional used) are also being increasingly valued. By addressing consumers' preferences, while complying with performance specifications this product is likely to have high acceptability in the market.

Conclusion. The cosmetic product developed addresses consumer's preferences and is unique in the market as it is eco-friendly, uses an autochthonous natural ingredient with key functional properties, has a comfortable and practical application ideal to provide relief and preserve skins' integrity.

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Conflict of Interest Statement. All authors are collaborators of Labfit-HPRD Lda (or were collaborators of the company at the time of the project). Labfit-HPRD Lda developed this product with marketing purposes.

References.

[1] E. G. Rodrigo, M. M. Gomes, A. Mayer-da-Silva, and P. L. Filipe, *Dermatologia. Ficheiro Clínico e Terapêutico*. .

[2] G. M. A. M. Esteves A. Juvenal, Baptista Poiares A., Rodrigo Guerra F., *Dermatologia*. .

[3] R. Gordon, A. M. Arikian, and A. S. Pakula, "Chilblains in Southern California: two case reports and a review of the literature," *J. Med. Case Rep.*, vol. 8, no. 1, p. 381, 2014.

[4] M. Ximena, “Eritema pernio: una enfermedad misteriosa,” vol. 27, no. 1, pp. 113–126, 2013.

[5] Joana Maria Almeida Mendes “Chilblains: a study about prevalence, solutions to address the issue in a established population in Portugal”. Master Thesis in Pharmaceutical Sciences. June 2016.

[6] Frazao, D.F., et al., Cistus ladanifer (Cistaceae): a natural resource in Mediterranean-type ecosystems. Planta, 2018. 247(2): p. 289-300.

[7] Gomes, P.B., V.G. Mata, and A.E. Rodrigues, Characterization of the Portuguese-Grown Cistus ladanifer Essential Oil. http://dx.doi.org/10.1080/10412905.2005.9698864, 2011.

[8] Raimundo, J.R., et al., Neglected Mediterranean plant species are valuable resources: the example of Cistus ladanifer. Planta, 2018. 248(6): p. 1351-1364.

[9] Śmigielski, K.B., et al., Comparison of qualitative and quantitative chemical composition of hydrolate and essential oils of lavender (Lavandula angustifolia). http://dx.doi.org/10.1080/10412905.2013.775080, 2013.

[10] Greche, H., et al., The Volatiles of the Leaf Oil of Cistus ladanifer L. var. albiflorus and Labdanum Extracts of Moroccan Origin and their Antimicrobial Activities. http://dx.doi.org/10.1080/10412905.2009.9700140, 2011.

[11] Tomas-Menor, L., et al., Correlation between the antibacterial activity and the composition of extracts derived from various Spanish Cistus species. Food Chem Toxicol, 2013. 55: p. 313-22.

[12] Guimarães, R., M.J. Sousa, and I.C.F.R. Ferreira, Contribution of essential oils and phenolics to the antioxidant properties of aromatic plants. 2020.

[13] Jordaan, H.F., “The diagnosis and management of perniosis (chilblains),” South African Fam. Pract., vol. 49, no. 6, pp. 28–29, 2007.

[14] Amberg N, Fogarassy C. Green consumer behavior in the cosmetics market. Resources. 2019;8(3):1–19

[15] Askadilla WL, Krisjanti MN. UNDERSTANDING INDONESIAN GREEN CONSUMER BEHAVIOR ON COSMETIC PRODUCTS: THEORY OF PLANNED BEHAVIOR MODEL. Polish J Manag Stud. 2017;15(2):7–15.