Rational design of Cosmetics with Thermal Water for Atopic Dermatitis

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Abstract

Background: Atopic dermatitis (AD) is a chronic remitting and relapsing inflammatory disease associated with atopy. AD therapy is aimed at controlling symptoms. Additionally, to the pharmacological approach and the reduction of precipitating factors of symptoms, AD management includes the use of adjuvant products that promote skin hydration and improve its protective barrier function. Thermal waters are widely used in various skin conditions. Two formulations were developed for application in AD whose core ingredient was thermal water through a safety and sustainability-driven rational design.

Methods: The supplemented thermal water was prepared through acold method and the lotion was formulated at low temperatures. For rheological characterization, a cone-plate viscometer was used and measurements were performed at 25º±2ºC during 1 minute. The cytotoxicity test of the main ingredient was performed using the MTT test on a human keratinocyte cell line (HaCaT).

Results: Both supplemented thermal water and body lotion presented homogenous appearance, good texture and absence of specific odor. Rheological characterization of body lotion highlighted its non-Newtonian, pseudoplastic fluid properties (for shear rate values of

37.50, 75, 150 and 337.50 (1/s) we obtained viscosities of 236.7, 156.0, 104.1, 62.64 cP respectively) with thixotropic behavior (negative hysteresis area).
Cytotoxicity testing upon keratinocytes revealed a very biocompatible profile of the core ingredient, maintaining cellular viability even at the highest tested concentration of 50% (v/v).
Conclusion: Design of a supplemented thermal water and a body lotion with Sao Pedro do Sul Thermal Water for atopic dermatitis was successfully achieved.

Keywords: Thermal water; Atopic Dermatitis; Barrier function; Body lotion; Supplemented thermal water

Introduction. Atopic dermatitis (AD) is a chronic and recurrent inflammatory skin disease, frequently associated with atopy. It is a chronic pruritic and inflammatory dermatosis, which progresses through crises. AD therapy aims to control symptoms, which includes the use of adjuvant products that promote skin hydration and improve its protective barrier function. The importance of proper skin care and the impact of topical application of products on AD has been increasingly highlighted. Numerous studies indicate that moisturizers have beneficial effects on AD clinical symptoms, transepidermal water loss, and stratum corneum hydration [1]–[6]. Bioactive properties of thermal waters have motivated their use in the prevention and treatment of various skin conditions, leading to their commercialization in the form of vaporizers or as ingredients of other cosmetic products [7].

We developed a range of innovative cosmetic products, including a supplemented thermal water spray and a body lotion through a rational design, by selecting ingredients that may promote well-being and barrier function of skin with atopic dermatitis (AD), using São Pedro do Sul Thermal Water as core ingredient. Furthermore, sustainability was included an attribute for development considering consumer's preferences and lifestyle trends.

Materials and Methods. The principles behind the development of these cosmetic products were based on criteria of minimalism, environmental sustainability, ease of use, innovation

in texture or presentation, long duration, and protection of the skin's microbiome to maintain its barrier properties.

Active ingredients such as humectants (Glycerin), skin repairers (Panthenol), antioxidants (Tocopherol) and prebiotics (Propylene Glycol, Water, Arctium Lappa Root Extract) were incorporated in the supplemented thermal water and body lotion formulas, thus giving them unique characteristics, compared to other products on the market. In the formula of the body lotion, we also added fatty esters of vegetable origin (Capric/Caprylic Triglycerides), actives that repair the skin barrier (Niacinamide), functional ingredients that mimic the natural moisturizing factor and with film-forming action (Water, Pentylene Glycol, Glycerin, Fructose, Urea, Citric Acid, Sodium Hydroxide, Maltose, Sodium PCA, Sodium Chloride, Sodium Lactate, Trehalose, Allantoin, Sodium Hyaluronate, Glucose), and vegetable oils (grape seed oil).

The supplemented thermal water was prepared using a cold method and the lotion was formulated at room temperature (25ºC), both pH values were adjusted to 4.9 respecting the recommended range of values for skin balance. For rheological characterization, a cone-plate viscometer was used, and measurements were performed under controlled temperature conditions (T=25 °C ± 2 °C) and for 1 minute (>5 cone revolutions). Cytotoxicity testing of the core ingredient, either alone or supplemented, was performed through MTT test upon a human keratinocyte cell line (HaCaT).

Student t-test was performed to compare the effect of each concentration with the respective control. p value <0.05 was accepted as denoting statistical significance.

Results. We have developed a moisturizing body lotion with a soft emollient composition with an advanced texture in a spray format for easier application, and a supplemented thermal water with a soothing and refreshing action. Different formulas were tested to achieve the ideal appearance, texture and performance. Final prototypes selected for the supplemented thermal water and the body lotion present homogeneous appearance, and no relevant odor. The supplemented thermal water presents a slight opaque appearance related to antioxidant and prebiotic ingredients. The body lotion has a white color with very smooth and nourishing

texture related to emollients and humectants ingredients. The application of the supplemented thermal water leaves a sensation of freshness and hydration on the skin. The body lotion is easy to spread, and its light texture allows it to be quickly absorbed, leaving a feeling of comfort on the skin.

Viscosity of the body lotion was identified as a key parameter for performance. Through rheological characterization it was classified as a non-newtonian, pseudoplastic fluid (for shear rate values of 37.50, 75, 150 and 337.50 (^{1}/s) we obtained viscosities of 236.7, 156.0, 104.1, 62.64 cP respectively) with thixotropic behavior (negative hysteresis area).

Cytotoxicity testing upon keratinocytes revealed a very biocompatible profile of the core ingredient, maintaining cellular viability even at the highest tested concentration of 50% (v/v). For the supplemented thermal water, a dose response was present with a decrease in cellular viability after 6.25% (v/v) (Figure 1). The high sensitivity of the method (cellular monolayer) may have contributed to this result since all ingredients were used at recommended concentrations for sensitive skin.

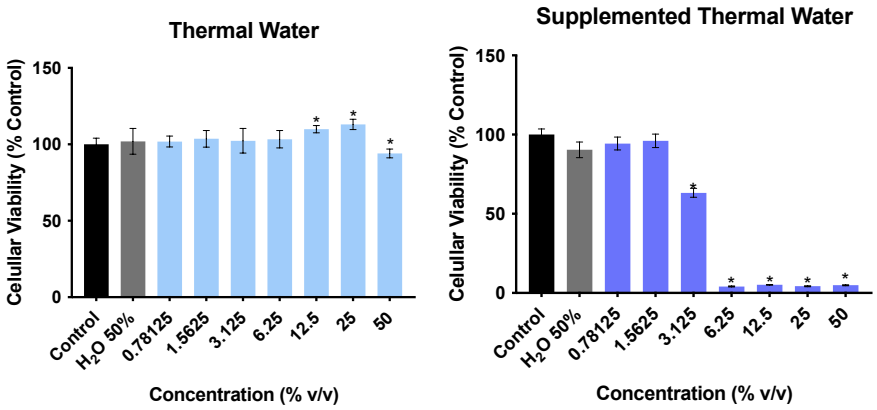

Figure 1 - Cellular viability profile (MTT assay; HaCaT – human keratonicyte cell line) for formulation São Pedro do Sul Thermal Water and the Supplemented Thermal Water formulation, ranging from 0.78% to 50% (w/v). Cell viability is represented as percentage of the control treated only with culture media. Results are presented as the mean values and bars represent standard deviations. Statistical Analysis: t- student test was performed for each concentration compared to control; * $p<0.05$ was considered a significant variation.

Discussion. Both the supplemented thermal water and the body lotion were developed with appropriate skin feel for application in atopic skin. Safety of both formulations is further supported by safety assessment calculations, according to the EC Regulation nº 1223/2009

based on each ingredient selected for these formulas and considering a high-risk application (impaired skin barrier function).

Trial results and long clinical experience have proven that emollients are safe and effective in patients with AD and that daily use of emollients on the skin decreases the risk of children developing AD by 30% to 50%. In addition, emollients should be used regularly as first-line therapy, even when no obvious skin lesions are observed. It should be noted that choosing an appropriate emollient for AD patients improves acceptability and adherence to treatment. In addition, regardless of the ingredients, patient preference and acceptance can influence the results of topical treatment, so we develop products that are easy to apply and that meet the needs of atopic skin to increase product acceptability [1], [6].

As some products already on the market, we chose to introduce actives that soothe itching and that present some anti-inflammatory action, with the aim of protecting the skin, avoiding inflammatory symptoms of AD that often result in reddish lesions and the use of topical corticosteroids. These active agents have been combined with emollients and humectants, providing repair and control of the skin barrier as well as xerosis [8], [9].

In addition, the core ingredient, thermal water proves to be essential for the overall added value of these formulations, being rich in essential minerals and having proven moisturizing and anti-irritant effects, which position it as a complementary approach in dermatological treatments [10].

Conclusion. The rational design of a supplemented thermal water and a body lotion with Sao Pedro do Sul Thermal Water for atopic dermatitis was successfully achieved. Textural and *in vitro* safety properties support further *in vivo* testing of these products.

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Conflict of Interest Statement. Ana Rita Gama was hired for the development of this funded project. Ana Sofia Oliveira has no relevant conflicts of interest related with this project. Ana Jorge, Liliana Gonçalves and Manuel António Campos are collaborators of Termalistur – Termas de São Pedro do Sul, E.M., S.A. Ana Palmeira de Oliveira and Rita Palmeira de Oliveia are collaborators of Labfit-HPRD Lda that provides services of cosmetic product development and production.

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