Shifting the perfume paradigm: A novel allergen-depleted fragrance composition provides anti-inflammatory effects *in vitro* and soothes xerotic skin *in vivo* to enhance patients' treatment adherence

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INTRODUCTION & OBJECTIVES

Fragrances are one of the most frequent causes of allergic contact dermatitis [1]. A pleasant scent, on the other hand, can significantly improve the cosmetic acceptability of moisturizers and, consequently, enhance patients' treatment adherence. Therefore, we developed a novel fragrance composition eliminating components of the baseline and fragrance series. Moreover, we investigated putative anti-inflammatory effects of the composition *in vitro* and a respective moisturizer formulation in a clinical study *in vivo*.

MATERIAL & METHODS

***In vitro* determination of anti-inflammatory efficacy of ingredients of the fragrance composition:** The reduction of Prostaglandin E2 (PGE2) and Interleukin-8 (IL-8) expression after applying a stressor substance was studied in human dermal fibroblasts and human epidermal keratinocytes, respectively.

Prostaglandin E2 (PGE2): Human dermal fibroblasts were stimulated with 100 ng/ml Lipopolysaccharides (LPS) to trigger PGE2 secretion. PGE2 concentration in the supernatant ± anti-inflammatory ingredients of the fragrance composition (0.001%, v/v) preincubation was measured after 24 h using a Prostaglandin E2 HTRF kit.

Interleukin-8 (IL-8): Human epidermal keratinocytes were stimulated with 10 ng/ml Tumor Necrosis Factor α (TNF-α) to induce the secretion of IL-8. After 24 h IL-8 concentration in the supernatant ± anti-inflammatory ingredients of the fragrance composition (0.001%, v/v) preincubation was determined using an IL-8 sandwich ELISA. The data were normalized on protein content. The effects of anti-inflammatory ingredients of the fragrance composition were shown by comparing cells incubated only with the stressor and the combination of stressor and the ingredients.

References: [1] Reeder MJ, 2020. Allergic Contact Dermatitis to Fragrances, Dermatol Clin 38, 371–377

***In vivo* razor Test:** Irritation on the volar forearms was provoked by shaving without lubricant on three consecutive days. The test product containing anti-inflammatory ingredients of the fragrance was applied to the shaved test area twice daily, whereas the control was left untreated. On Day 4, skin redness was assessed both by self-grading as well as measured using a Chromameter.

Clinical patient preference study: Evaluation of the consumer acceptance of a skin care formulation containing the novel allergen-depleted fragrance versus the unscented version of the formulation after 2 weeks of regular usage by 86 patients (age 25-75 years) suffering from dry skin.

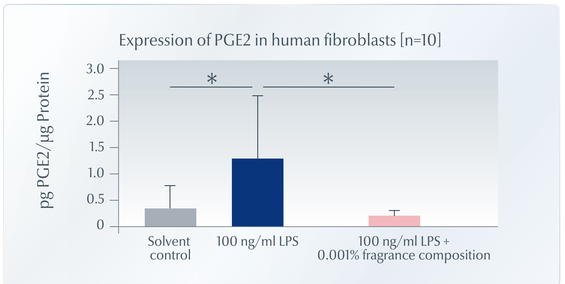

Figure 1a: Expression of PGE2 (n=10) of human dermal fibroblasts. 100ng/ml LPS significantly induces the expression of PGE2. The addition of anti-inflammatory ingredients of the fragrance composition (0.001%,v/v) leads to a significant reduction of PGE2 expression (*= p<0.05). Data were normalized on protein content.

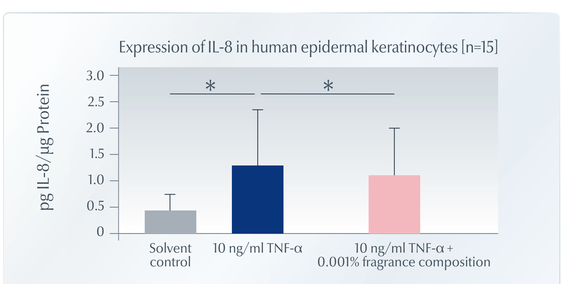

Figure 1b: Expression of IL-8 (n=15) of human epidermal keratinocytes. 10 ng/ml TNF-α significantly induces the expression of IL-8. The addition of anti-inflammatory ingredients of the fragrance composition (0.001%, v/v) leads to a significant reduction of IL-8 expression. (*= p<0.05) Data are normalized on protein content.

RESULTS

***In vitro* determination of anti-inflammatory efficacy of ingredients of the fragrance composition:** The expression of PGE2 (figure 1a) as well as of IL-8 (figure 1b) was significantly (*= p<0.05) reduced by the anti-inflammatory ingredients of the fragrance composition compared to the stressed samples.

***In vivo* razor Test:** Skin redness of razor-stressed skin was significantly reduced in the treated skin area compared to the untreated area as shown both by objective measurements (figure 2a) and self-grading (figure 2b) .

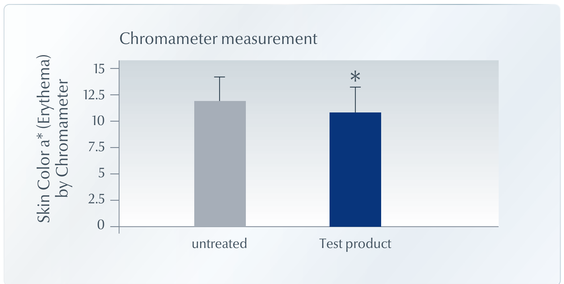

Figure 2a: Chromameter measurement on day 4. Higher a*-values correspond to increased skin redness. Application of the moisturizer significantly reduces measured redness (*= p<0.05). Irritation on the volar forearms was provoked by shaving on three consecutive days. The moisturizer containing the anti-inflammatory fragrance composition was applied to the shaved test area twice daily, whereas the control was left untreated.

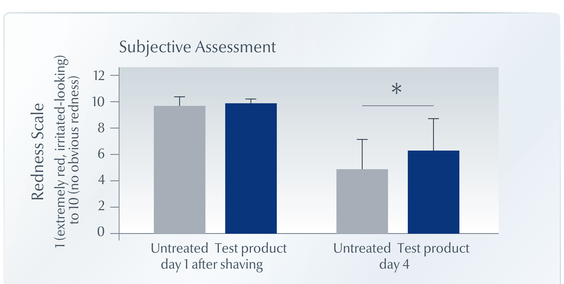

Figure 2b: Subjective Self-grading: Higher values correspond to less redness and improved skin conditions. Shaving the forearms on three consecutive days visibly induces irritation, compare untreated Day 1 to Day 4. Application of the moisturizer significantly reduces perceived skin irritation and redness (*= p<0.05).

Clinical patient preference study: Evaluation of the acceptance of the scented lotion by dry skin sufferers currently using the unscented version (figure 3) showed that 97% agree that with the scented formulation it does not feel for them like they have to apply something on their skin but they also enjoy it. 91% confirmed that the scented lotion makes their care routine more pleasant. Furthermore, 71% of the patients confirm that they like the scented product better than the unscented version they used.

Figure 3: Subjective assessment (n=86) of the moisturizer containing the allergen-depleted, anti-inflammatory fragrance composition by dry skin patients

CONCLUSION

The novel, allergen-depleted fragrance composition provided distinct anti-inflammatory effects in epidermal and dermal cell cultures *in vitro* and its incorporation in a moisturizer formulation resulted in clinical amelioration of experimentally induced skin irritation *in vivo*. Moisturizers based on the novel fragrance composition may provide an improved treatment option for patients and doctors seeking safe but pleasant skin care formulations which, moreover, actively soothe inflammatory skin conditions. Hence, the long-standing paradigm of fragranced moisturizers considered as allergenic risk in the treatment of xerotic dermatoses may soon become obsolete. Conversely, the tested allergen-depleted fragrance can actively enhance patients' treatment adherence and may complement topical anti-inflammatory medications.

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