"Relevant technologies to develop future sunscreen products with longer and safer photoprotection"

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Abstract

The importance of developing innovative and effective sunscreens is critical in the Dermatology and Cosmetic fields, becoming even more crucial with global climate changes and the increasing incidence of skin cancer. There is a constant effort for the development of innovative sunscreens, a challenging task as those formulations should provide the highest skin protection while being safe and sensory pleasant for daily use without causing environmental alterations.

The use of organic UV filters, even though present great cosmetic advantages have negative odds. Indeed, they can penetrate the skin; be photo-unstable, require frequent re-application and impact significantly the marine environment. The current recommendation for effective use of sunscreens is re-applying every two hours. Previous studies conducted in our research group showed that in a 2-hour window the organic UV filters presented a significant reduction in their presence on the skin surface already observed 30 minutes after sunscreen application. UV filters penetration inside the skin was also confirmed in those studies. Encapsulation, film formers or skin bio-adhesive technology are relevant examples which will improve significantly the efficacy and the safety of future sunscreen products.

Vibrational Spectroscopic techniques were used to investigate some of these different technologies applied on sunscreens formulations. In this study, we used the Confocal Raman Spectroscopy and ATR-FTIR spectroscopy in-vivo to evaluate and compare their efficacy as well as their safety profile. Associated with 3D face mapping we showed the retention profile of the UV filters around the face over time as well as their penetration profile inside the stratum corneum. Our data showed that encapsulation technology, or the use of film formers improved the retention of organic UV filters on the skin surface, increasing the sunscreen efficacy and prevented the penetration of these UV filters in the skin, limiting their toxicological risks. These results were validated during pre-clinical trials.

The technologies presented in this study allowed a higher and longer retention of UV filters at the skin surface increasing their effectiveness and drastically reducing their toxicity. The 3D mapping based on spectroscopic measurements provides an innovative communication approach to highlight the benefits of future sunscreen formulation to consumers.

1. Introduction

The importance of developing innovative and effective sunscreens is critical in the Dermatology and Cosmetic fields. Global climate changes, pollution and increasing scientific knowledge are contributing to making sunscreen essential in our life to prevent sun damages and more aggressive skin alterations like sunburn and in the worst-case skin cancer [1]

There is a constant effort for the development of innovative sunscreens, a challenging task as those formulations should provide the highest skin protection while being safe and sensory pleasant for daily use without causing environmental alterations [2].

The organic UV filters, although present great cosmetic advantages have several negative side effects. Indeed, they can penetrate the skin; be photo-unstable, require frequent re-application and impact significantly the marine environment [3], [4], [5].

The current recommendation for effective use of sunscreens is re-applying every two hours. Previous studies conducted in our research group showed that in a 2-hour window the organic UV filters presented a significant reduction in their presence on the skin surface already observed 30 minutes after sunscreen application. UV filters penetration inside the skin was also confirmed in those studies. Encapsulation, film formers or skin bio-adhesive technology are relevant examples which can improve significantly the efficacy and the safety of future sunscreen products.

Within this frame of reference, there are several alternatives that can improve the sunscreen photoprotection with a better skin retention, more uniform distribution and reduce the risk of penetration through the skin. Indeed, the use of specific ingredients in the formulation, as film former polymers is one interesting alternative, that can improve the sunscreen performance [6], [7], [8]. The use of encapsulated UV filters is another alternative that can reduce the risk of toxicity associated with organic sunscreens as it can reduce the risk of penetration and also can improve the UV filters distribution on the stratum corneum and stability [9].

Current organic UV filters do not remain effective for long and considering the recommendation is to keep re-applied every two hours, it should be taken into consideration that their efficacy can be improved. Moreover, studies have been trying to understand the risk of penetration the skin beyond the stratum corneum region, which is related to the safety of those formulations [10], [11].

In this context, the aim of the present study was to evaluate 3 different sunscreen formulations containing a combination of 3 different organic UV filters, octocrylene, avobenzone and homosalate in regular formulation, associated with a film former ingredient or in an encapsulated form. I*n vivo* confocal raman system was used to evaluate the UV filters penetration profile inside the skin while *in vivo ATR*-FTIR spectroscopy was used to evaluate the UV filters distribution and retention on the face overtime.

2. Materials and Methods

<u>Sunscreen Formulations</u>

The sunscreen formulations used in this study were developed based on the following ingredients: cetearyl alcohol, glyceryl stearate, C12-15 Alkyl Benzoate, Bis-PEG/PPG-20/5 PEG/PPG-20/5 Dimethicone (and) Methoxy PEG/PPG-25/4 Dimethicone (and) Caprylic/Capric Triglyceride, Caprylic/Capric Triglyceride, BHT, Propylene glycol, EDTA and Water.
The organic UV filters used were avobenzone at 3% concentration, octocrylene 10% concentration and homosalate at 15% concentration. The final formulas contained the UV filters in regular forms (*free*) or associated with a film former ingredient (Polyamide-3), or in encapsulated forms.

Confocal Raman measurements

For this study, 5 subjects were selected and a series of 8 Confocal Raman spectroscopic lines on the face area were scanned into the skin at 5-micron steps for 15 microns deep. Confocal Raman images were acquired using a SkinProbe system from Horiba, a confocal Raman microscope equipped with a 660nm laser and developed for clinical evaluation.

The Spectral parameters used to scan the skin samples were:
Laser frequency: 660 nm
Laser power: 100 mW
Acquisition time: 1 exposure at 5 seconds/spectrum
Spectral range: 4000-400 cm^{-1}

Spectroscopy analysis

The hyperspectral images were analyzed using Isys Chemical Imaging analysis 5.0 software (Malvern Instruments Limited, Malvern Works, UK).
For the confocal Raman measurements, the band at 2200 cm^{-1} was used to investigate the octocrylene. For the avobenzone we used the band at 1605 cm^{-1} for the homosalate the band at 2924 cm^{-1}. Spectra were normalizated to the amide 1 band.
The spectroscopic data were used to construct a 3D mapping of the UV filter distribution on the face overtime. For statistical analysis the same area values were used on ANOVA test using GraphPad Prism 8 software (San Diego, California, United States).

3. Results

3D mapping showing the distribution on the face of the octocrylene over time related to 3 different formulations showed that the free form of the UV filters alone presented a less uniform distribution around the face and a significant lower level of cotocrylene (**figure 1**) compared to the formulations with film former or encapsulated UV filters. The highest and longest retantion of octocrylene was observed with the encapsulated technology. The concentration of octocrylene decreased along the timepoints evaluated with the free fromulation, the decrease was less pronouce with the film former and almost non-existent with the encapsulted UV filters(**Figure 2**). The decrease of the octocrylene at the skin surface can be related to the degradation of the sunscreen overtime and/or to the penetration of the UV filters inside the skin.

A significant amount of octocrylene penetrated inside the skin 2 hours after topical application of the free form sunscreen. The encapsulated octocrylene prevented its penetration inside the skin. For the skin penetration evaluation using in vivo confocal raman, it was observed the presence of octocrylene up to 15µm inside the skin, which means that with the free sunscreen formulation the octocrylene can penetrate bellow the stratum corneum region.

When comparing these results with the two other formulations, the addition of the film former ingredient was able to improve the distribution of the formulation resulting in a more uniform profile observed by the 3D mappings constructed. The film former ingredient also allowed to reducte the penetration of UV filters insie the skin.

Finally, the sunscreen with the encapsulation technology promoted minimum penetration in the skin, presenting a uniform profile and also a more intense retention overtime when compared to the free form.

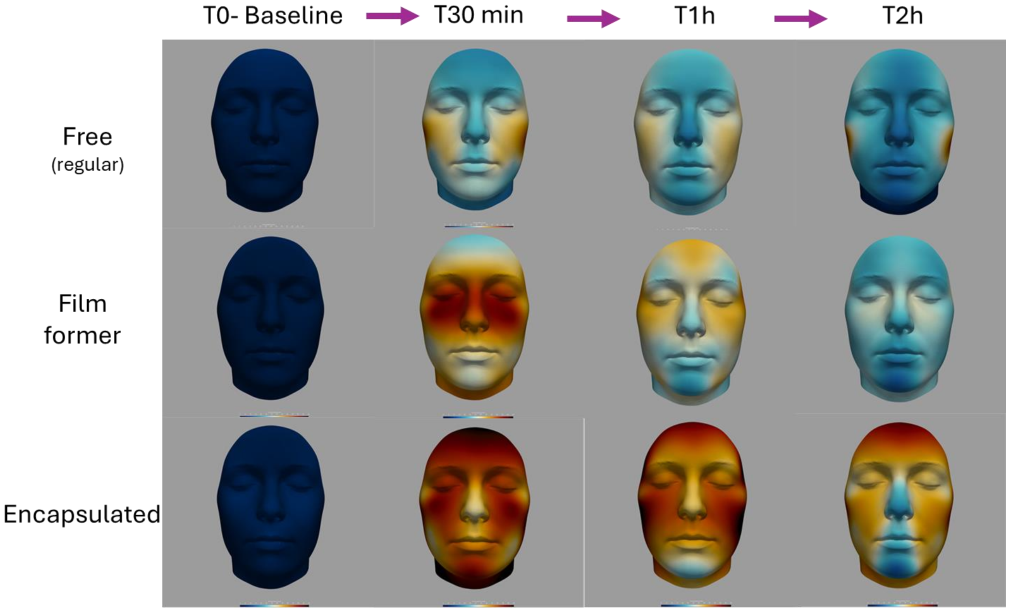

Figure 1: 3D mapping showing the distribution on the face of the octocrylene over time related to 3 different formulations: regular UV filters (free), associated with a film former ingredient or using encapsulated forms. The 3D maps were generated based on the in vivo ATR-FTIR measurements. The highest amount of octocrylene appears in red while the dark blue represents no octocrylene.

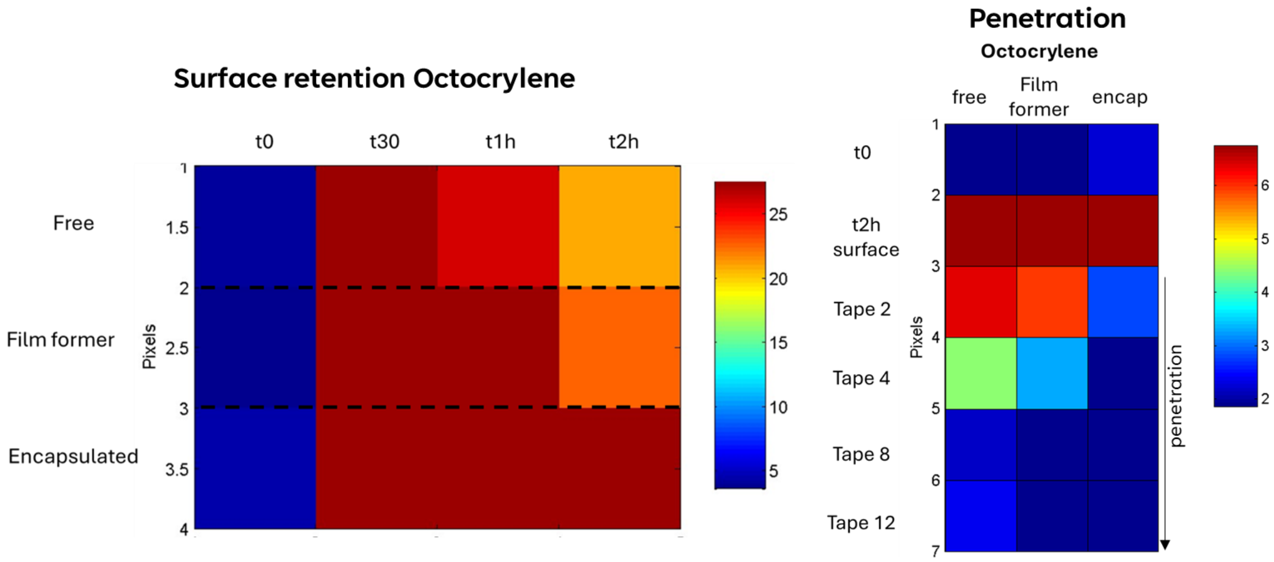

Figure 2: In vivo ATR-FTIR data showing (left) retention of octocrylene at the skin surface over time related to the 3 different formulations, (right) penetration of the octocrylene inside the skin 2 hours after topical application of the sunscreen.

4. Discussion

UV filter penetration is an important concern for research and this outcome should be taken into consideration in the development of sunscreen products especially with the importance of the daily use of sunscreen. Studies support the safety concern associated with sunscreens penetration [10], [11]. In the present study it was possible to observe an improvement in the UV filters distribution and the UV filters retention at the skin surface in suncreens formulated with a film former or using encapsulated UV filters. These technologies promote a more uniform distribution and a stronger retention of organic UV filters on the stratum corneum first layers.

The UV filters under study were the most commonly used in commercial formulations and the results showed that all 3 evaluated UV filters presented penetration below the first layers of stratum corneum region, which is not a desirable effect for sunscreen formulations. Meanwhile the two different technologies applied in this study (encapsulation and film former) provided an improvement in the safety profile, which show the benefits of the application of those technologies in the research and development of new sunscreen formulas [6], [7], [8]. The data presented in this study showed the spectroscopic methods can be used to investigate and improve the stability, efficacy and safety profile of sunscreen formulations

The findings recroded in vivo by Confocal Raman study correlate well previous studies using *ex vivo* confocal raman, and ATR-FTIR spectroscopy. The free form presented agglomerates in the skin, which is related to a heterogenous distribution of UV filters at the skin surrface, which can consequently affect the product UV protection [12], [13].

The film forming technique is aimed to improve the uniformity of the formulation as well as the retention of the UV filters on the skin, which was found to be partially true. The obtained results showed an improvement in the distribution, and an improvement in the retention but the encapsulation technology promoted a more significant improvement in both factors. Previous studies from our research group also showed that encapsulation can lead to sunscreens less susceptible to degradation, which is also another advantage related to this technology [9].

The in vivo study, along with the depth profile observation of those formulations promoted a comprehensive view of the sunscreen interaction with the skin and how the application of different technologies can support the development of safer sunscreen products with higher efficacy.

5. Conclusion

The 3D mapping based on spectroscopic measrumnets present an innovative communication approach for the consumer highlighting the benefits of innovative technologies (encapsulation, film former) in the sun protection field. The technologies tested in this study allowed to increase the retention of UV filters, increasing their effectiveness and drastically reduce their toxicity. Safer and more efficient sunscreen are within reach. This work also shows spectroscopic techniques are suitable clinical methods to evaluate sunscreen products.

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7. References

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