Enlarged photoprotection efficiently covering the whole UV spectrum: evaluation of long term clinical anti-aging benefits in a real life split-face study

Flament, Frederic[1]; Mercurio, Daiane[2*]; Bernerd, Françoise[1]; Tricaud, Caroline [1]; Jager-Lezer, Nathalie [1]; Josso, Martin [1]; Muller, Benoit [1]; Alves, Marcelli [2]; Delaunay, Caroline[1]

1 L'Oréal Research and Innovation, France;

2 L'Oréal Research and Innovation, Brazil;

**Daiane Garcia Mercurio, daiane.mercurio@rd.loreal.com*

Abstract

The objective of this study was to evaluate *in vivo* and in real sun conditions global anti-aging benefits of a broader UVA1 protection, up to 400 nm, with the split-face daily application of a sunscreen formulation enriched with Methoxypropylamino Cyclohexenylidene Ethoxyethylcyanoacetate. For this purpose, fifty-two healthy female volunteers, phototypes I-III, aged between 35-65 y.o. were enrolled in a double blind, split-face clinical study in Brazil. After 2 weeks of wash-out, a sunscreen enriched with MCE 1% (SPF 50+) with an absorption profile covering the longest UVA wavelengths, up to 400nm, and a reference state-of-the-art sunscreen (SPF 50+ without MCE) were applied half-face twice daily with controlled application for one month. The volunteers were sun exposed for up to two hours daily and they had standard pictures acquisition and clinical aging signals evaluation using Skin Aging Atlas at baseline and after one month. The results showed that MCE enriched sunscreen improved significantly crow's feet wrinkles, upper lip wrinkles, ptosis, texture of the mouth contour, upper lip texture and whole face pigmentation when compared to baseline and to the reference formula after one month. In addition, MCE sunscreen presented significantly better results vs the reference for lateral facial pigmentation and upper lip pigmentation. In conclusion, the sunscreen containing MCE filter presented superior anti-aging benefits compared to the state-of-the-art broad-spectrum sunscreen. For the first time we proved that efficiently covering the whole UV spectrum with MCE UV filter, succeeded in better preventing and reducing skin photodamage signs in real sun exposure conditions.

Keywords: Methoxypropylamino Cyclohexenylidene Ethoxyethylcyanoacetate; Photoprotection; anti-aging; UVA1 protection

Introduction

UVA1 rays (340–400 nm) account for at least 75% of ultraviolet wavelengths reaching the Earth. They are able to induce epidermal and dermal damage and contribute to immunosuppression, carcinogenesis, hyperpigmentation and photoaging [1-5]. Today, state-of-the-art sunscreen formulas can efficiently filter UV wavelengths up to 370/380nm, but have limited absorption in the 370/380–400 nm wavelengths range. This way, with current sunscreen formulations, the skin is still not efficiently protected from the last 20nm UVA1 range, therefore being accessible to UV damage caused by this specific wavelength range.

Recently, a new cyclic merocyanine UVA1 absorber, Methoxypropylamino Cyclohexenylidene Ethoxyethylcyanoacetate (MCE) (S87), exhibiting a maximal peak of absorption at 385 nm (Figure 1) was approved by the Scientific Committee on Consumer Safety (SCSS) and listed in the Annex VI of EU authorized UV filter for use in sunscreen products, allowing for the first time, the development of sunscreen formulations covering effectively the complete UVA1 band.

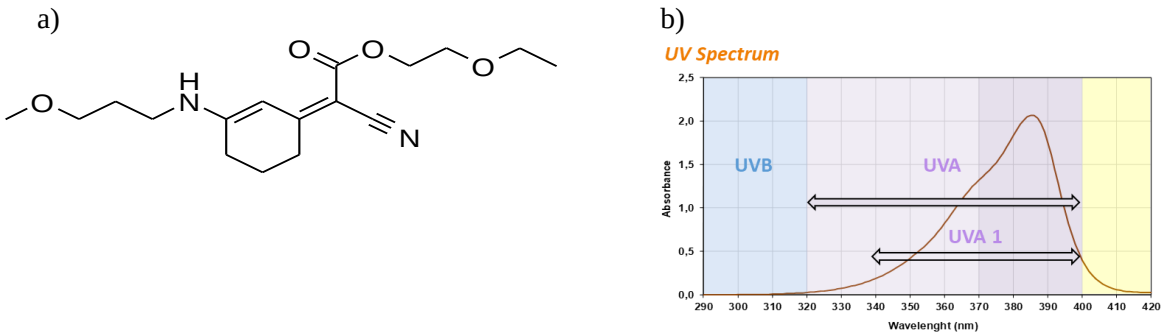


Figure 1. Characteristics of the MCE - Methoxypropylamino Cyclohexenylidene Ethoxyethylcyanoacetatfilter. (a) Structural and (b) absorption characteristics. Absorption spectrum of the MCE filter measured using a spectrophotometer by a 1-cm path length cuvette at 10 mg/l solution or by a 1-mm cuvette at 100 mg/l (measured absorbance every 5 nm).

The extra protection benefits provided by MCE was proven by a series of laboratory testing in controlled UV exposure conditions. Using a reconstructed skin model, formulations improved by addition of MCE enabled significantly higher UVA1 protection of the epidermis and the dermis, with a better protection against dermal fibroblasts death, UVA1-induced gene and protein expression modulations in fibroblasts and keratinocytes. When submitted to controlled UV exposure *in vivo*, MCE enriched formulations showed a significantly higher anti-pigmentation efficacy when compared to state-of-the-art formulation [6].

These results demonstrated the great potential of extended UVA1 protection on skin damage prevention, in standardized conditions; however, until now, there was no evidence of the added benefits of

efficiently covering the whole UV spectrum on global skin photoaging face signs, *in vivo* and in real sun exposure conditions. Thus, this study brings the important contribution of a robust clinical study protocol, split-face design, to validate the benefits of daily protection enlarged in the range 380 – 400nm measured by objective evaluation of photoaging signs.

Objective

The objective of this study was to evaluate *in vivo* and in real sun conditions global anti-aging benefits of a broader UVA1 protection with the split-face daily application of a sunscreen formulation enriched with MCE compared to the state-of-the-art reference sunscreen.

Methodology

After Ethical Committee approval, fifty-two healthy female volunteers, phototypes I-III, aged between 35-65 y.o. were enrolled in a double blind, split-face clinical study in Brazil (Campinas – SP) from September to December 2019. After 2 weeks of wash-out, a sunscreen enriched with MCE 1% (SPF 50+) [MCE] with an absorption profile covering the longest UVA wavelengths, up to 400nm (Figure 2), and a reference state-of-the-art sunscreen (SPF 50+ without MCE) (Reference) were applied half-face twice daily with controlled application for one month.

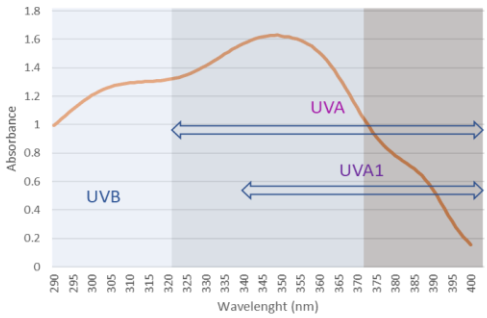


Figure 2: Absorption spectrum of the MCE enriched formulation. The formula absorption spectrum (290−400 nm) was obtained using a spectrophotometer. The formula was dissolved in isopropanol using quartz cell of 0.2cm path length.

The study flow consisted of daily visits at the research center with up to 8 steps for controlled product application, sun exposure and skin evaluation. The volunteers were sun exposed to up two hours daily according to the flow described at Figure 3.

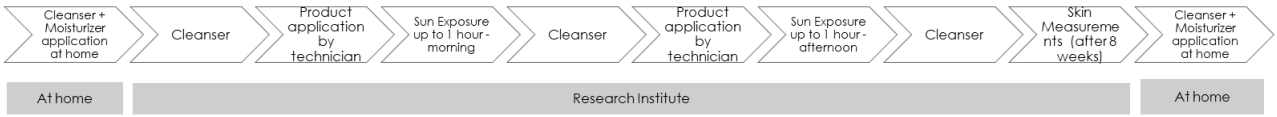
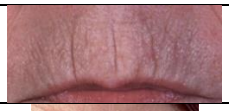
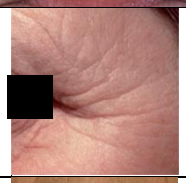
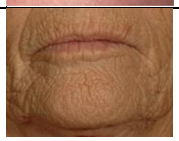
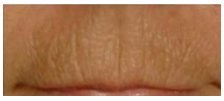
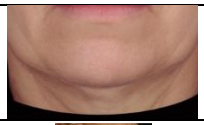
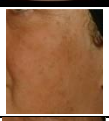
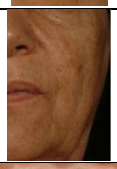
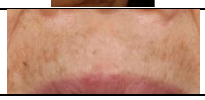


Figure 3: Study flow during the study. The volunteers visited the investigational research center daily for product application, sun exposure and skin evaluation for some time-points.

The study subjects had standard pictures acquisition and clinical aging signs evaluation using Skin Aging Atlas by a trained expert panel [7,8] (Table 1) at baseline and after one month. The statistical analysis was performed comparing MCE enriched formulation results with the reference sunscreen and vs baseline.

Table 1. Facial signs relative to wrinkles and skin texture, ptosis and pigmentation disorders and their photographic illustrations.

Clinical Signs	Definition	Scale	Visual
Upper lip wrinkles	Depth of the deepest wrinkle at upper lip zone (lip surface excluded). ‘	0–6	
Crow’s feet wrinkles	Depth of deepest wrinkle at the area of outer eye corner (5mm at least outside from the corner).	0–6	
Texture of mouth contour	In addition to dimples, chin, cheek and upper lip areas have a thick skin appearance, are padded, and have a pronounced micro-relief forming a grid.	0–7	
Upper-lip Texture	In addition of vertical lines more or less deep, upper lip has a thick aspect, padded and has a pronounced microrelief forming a grid.	0–6	
Ptosis of the lower part of the face	Sagging severity of the lower part of the face on each side of the chin.	0–5	
Lateral facial pigmentation	Severity of pigmentation disorders on pigmentary spots on external lateral area of the face.	0–5	
Whole-face pigmentation	Density of pigmentation disorders on all the face.	0–5	
Upper-lip pigmentation	Hyperpigmentation of the upper lip giving a “burn” aspect to the skin.	0–7	

Results and Discussion

This study investigated the visible photoaging signs impact of the enlarged protection in the 380nm – 400nm in real sun conditions. Owing to its absorption peak at 385 nm, MCE addition in a state-of-the-art reference formula allowed the formulation of this new domain on UV protection, UVA1 enlarged protection up to 400nm.

With this new technology, our results proved that the enlarged protection provided better results on photoaging signs such as pigmentation, texture and wrinkles in the population studied compared to the state-of-the-art sunscreen formulation and compared with baseline conditions. The assessment by Skin aging Atlas showed that MCE enriched sunscreen improved significantly crow's feet wrinkles, upper lip

wrinkles, ptosis, texture of the mouth contour, upper lip texture, whole face pigmentation, lateral facial pigmentation and upper lip pigmentation vs the sunscreen reference (Figure 4).

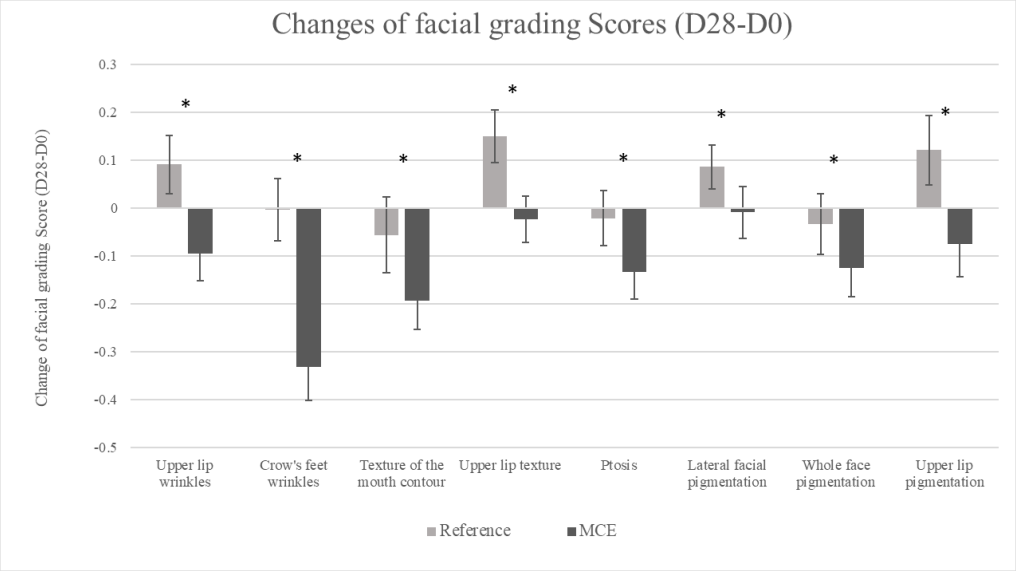


Figure 4. Changes in facial grading scores obtained before and after 28 days for the 2 groups: MCE Enriched sunscreen formula (MCE) and State-of-the-art Sunscreen (Reference). Mean ± 95% Confidence Interval. * Significantly different from reference formulation $p<0.05$.

Considering the time-effect, the region treated with MCE enriched sunscreen also improved skin photoaging signs after 1 month, presenting significant reduction on crow's feet wrinkles, upper lip wrinkles, ptosis, texture of the mouth contour, upper lip texture, whole face pigmentation and vascular disorders in comparison to baseline values (Table 2).

Table 2. MCE facial grading scores obtained at baseline and after 28 days for the 2 groups: MCE Enriched sunscreen formula (MCE) and State-of-the-art Sunscreen (Reference). Mean ±95% Confidence Interval.

		Upper lip wrinkles	**Crow's feet wrinkles**	**Texture of the mouth contour**	**Upper lip texture**	**Ptosis**	**Lateral facial pigmentation**	**Whole face pigmentation**	**Upper lip pigmentation**
MCE	D0	1.41± 0.10	3.03±0.09	1.38±0.08	1.49±0.08	2.46±0.08	1.30± 0.07	1.34± 0.07	1.26±0.09
	D28	1.31± 0.09	2.69±0.10	1.19±0.07	1.47±0.07	2.33±0.08	1.29±0.07	1.22±0.07	1.18± 0.08
	p value	**< 0,0001**	**< 0,0001**	**< 0,0001**	NS	**< 0,0001**	NS	**< 0,0001**	**0.012**

It’s well known in the literature that daily use of broad-spectrum sunscreen is effective to prevent photoaging related signs [9-11]. Now, we could prove that an efficient filtration/absorption extended in the 380-400 nm range, can lead to a higher performance for daily photoprotection routines. These results translate in real sun exposure conditions, close to real life, the effective protection mechanisms described in controlled UV exposure conditions. These clinical benefits can be linked to the effective protection of MCE on some biological mechanisms, such as the prevention of oxidative stress and UVA-induced gene expression modulations. UVA1 rays’ main mode of action is the generation of reactive oxygen species,

leading to oxidative damage to cellular components such as DNA, lipids, and proteins and subsequent biological pathways activation. Due to high penetration properties of these UVA1 rays, the biological consequences can be observed up to the dermis, supporting their role in photoaging process. In addition, UVA-induced pigmentation is a key factor for hyperpigmented disorders due to sun exposure. Thus, these biological mechanisms underlying the new technology performance can be linked to impact at skin surface properties such as texture, wrinkles visibility and pigmentation disorders improvement [6].

This study brings an important contribution showing the one-month effect using this new technology on visual signs in Caucasian skin panel with phototypes I to III and opens new possibilities of investigation as studying the effects on darker phototypes, *in vivo* morphological and structural evaluation of epidermis and dermis and studies with longer duration.

For the first time, thanks to MCE filtering properties and to an assertive clinical study protocol, we've proven a higher efficacy with a broad spectrum photoprotection enlarged in the longest UVA1 wavelengths 380-400nm. The data strongly supports the benefits on daily usage of MCE enriched sunscreens on improvement of photoaging markers and showcases additional anti-aging benefits for the consumers from the state-of-the-art sunscreen products.

Conclusion

In conclusion, the sunscreen containing MCE filter presented superior anti-aging benefits compared to the state-of-the-art broad-spectrum sunscreen. For the first time we proved that efficiently covering the whole UV spectrum with MCE UV filter, succeeded in better preventing and reducing skin photodamage signs in real sun exposure conditions.

Conflict of Interest Statement. The authors are employees of L'Oréal Research and Innovation,

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