

Effect of a new cosmetic formulation on reducing cutaneous pigmentation: a clinical and biometrological approach

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Introduction

During the last few years, a number of discoveries have enabled the cellular occurrences that control melanogenesis to be better understood. It has been shown that the positive regulation of pigmentation is influenced by three pathways of major intra-cellular signals constituted by the AMPc relayed by the protein kinase A (PKA), the protein kinase C (PKC) and nitrogen monoxide(NO) (Fig. 1).

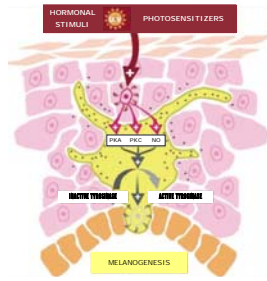


Figure 1 : Cellular events of melanogenesis

The activation of PKC is an initial and predominant intra-cellular stage of melanogenesis. Directly stimulated by UV rays, PKC stimulates the proliferation of melanocytes, their dendricity (the transport of melanin to the keratinocytes) and melanogenesis (stimulation of the tyrosinase). For its part, PKA is activated via alpha-MSH and in turn stimulates the tyrosinase. In order to give a specific reply to the problems of hyperpigmentation, a new and patented depigmenting formula was developed and based on: - a new patented inhibitor of PKC that is the result of the joint research of the Laboratoires Expanscience and a CNRS team (ESIP - UMR 6503 - Pr Barrault) which is specialised in green chemical catalysis: the cycloceramide (undecyl-dimethyl-oxazoline) that belongs to the family of 2-oxazolines.

This active ingredient have shown a significant down regulation of the production of melanin in vitro with or without the stimulation of UV light. - a PKA inhibitor: Sepiwhite (undecylenoylphenylalanine); - an anti-free radicals complex, inhibitors of NO in the form of a cocktail of vitamins (C + E).

The aim of this clinical study was to evaluate the effectiveness of the global depigmenting agents of this new cosmetic formula by using, as a model of hyperpigmentation, facial melasma in women with a high phototype (between IV and VI).

Protocole

This open monocentric study was carried out at the Centre Laser Dermatologique (CLD) in Marseille, over a period of 120 days, with three evaluation points (D0 = T0, D60 =T1 and D120 = T2). 20 females volunteers aged over 18 and of phototypes IV to VI, who had a facial epidermic melasma (Woods light) that had been stable for 6 months and in existence for less than 10 years, were included. The product tested was applied twice a day on the hyperpigmented zone. A sunscreen with an index of 50 was applied once or twice a day throughout the study.

Evaluation criteria (T0, T1 and T2)
-Simplified MASI score (Kimbrough-Green et al. Arch Dermatol 1994; 130: 727-733). (Melasma Area and Severity Index) = (D+H)XA (Area = A, Darkness = D, Homogeneity = H).

-Melanic Index by MX 16 Mexameter (Courage and Khazaka) on two hyperpigmented zones and two healthy zones on each side. It explores the wavelengths of specific absorption of the two principal chromophores, melanin and haemoglobin and is directly linked to epidermic melanisation.

-Quality of Life using the MELASQOL scale (Bakrishnan R et al. Br J Dermatol 2003 149 (3) 572-7).

-Self-evaluation questionnaire delivered by the psychometric apparatus PS24 (Psycho-Log24R).

-UV photographs with image analysis. The image obtained is posterised (reduction of the numbers of colours in an image) at two different levels: 4 and 8. A reduction in the stains leads to an improved distribution of the levels of grey and this is reflected in an increase

in the number of pixels. In the same way, the surface index examines the proportion of the non-dyschromic surface of a given zone. If it increases, this indicates a regression in the surface area of the melasma.

-Safety

-Statistics : non-parametric Wilcoxon test on paired samples.

Results

DEMOGRAPHY

19 volunteers were present at the end of the study; aged 20 to 61 years (mean 42.7 years): 5 phototype IV, 13 phototype V and 1 phototype VI.

MASI SCORE (Fig. 2).

Statistical improvement is noticed at T1/T0, T2/T0 and at T2/T1 with a reduction in the MASI score of 23.7% (p < 0.0022). The clinical effect is therefore clear and significant from the 60th day onward and continued up to the 120th day.

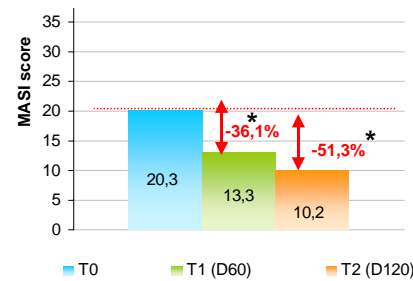


Figure 2 : MASI evaluation * statistically significant difference

MELANIC INDEX (table 1)

	Healthy skin	% decrease	Healthy skin Statistics	Melasma	% decrease	Melasma Statistics
T0	500,25			520,35		
T1/T0	500,08	0,03%	NS	513,92	1,24%	* p = 0,0066
T2/T0	503,53	0,65%	NS	514,79	1,07%	* p = 0,0382

Table I: Melanic index NS = Non Significant * : statistically different

MELASQOL (Fig. 3).

The initial results show the considerable impact of melasma on the quality of life of the patients (maximum overall score is 1000).

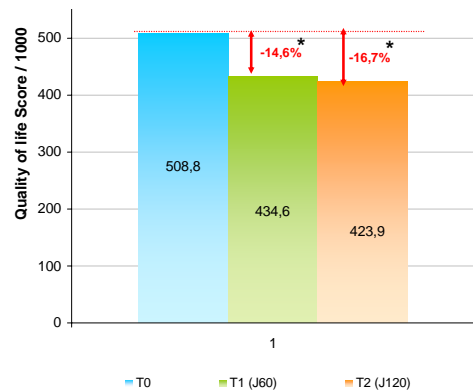


Figure 3 :Evaluation of quality of life

* Statistically significant difference

AUTO-EVALUATION (Table II, Fig. 4).

The product tested procured significant improvement (>50%) in the facial complexion at T1 and T2

	% improvement	Statistics	% improvement	Statistics
	T1/T0	T1/T0	T2/T0	T2/T0
Clarity	+60,6%	*	+48,1%	*
Brightness	+82,2%	*	+87,4%	*
Uniformity	+65,7%	*	+61,4%	*
Transparency	+69%	*	+59,7%	*

Table II: Results of the psychometry apparatus PS24 concerning complexion * : statistical significance according to the Wilcoxon test.



Figure 4 : Efficacy auto-evaluation (spot's intensity, surface and number)

* Statistically significant difference

UV PHOTOGRAPHS WITH IMAGE ANALYSIS (Fig. 5)

For each test zone retained, the number of pixels for each level of grey was counted, on the right and on the left and at posterisation levels of 4 and 8. The photographs show an example of posterisation level 4 which illustrates clearly the attenuation of contrast, the fractioning of the pigment and therefore, in all, an attenuation of the stains compared with adjacent skin.

The study of the distribution of levels of grey in the image therefore shows an improvement with better distribution and thus an image with less contrast. The intensity of the colour of the melasma is attenuated compared with the surrounding skin.

All the results that use 8 levels of grey were significant at T2. (Figure 6)

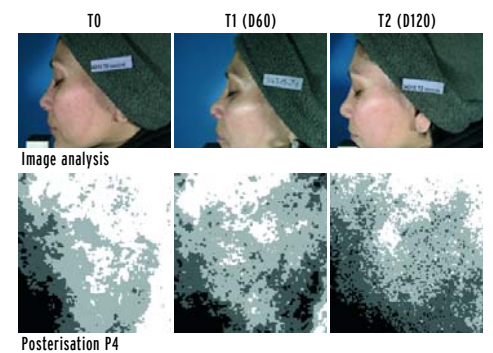


Figure 5 : UV photographs with image analysis (posterisation 4)

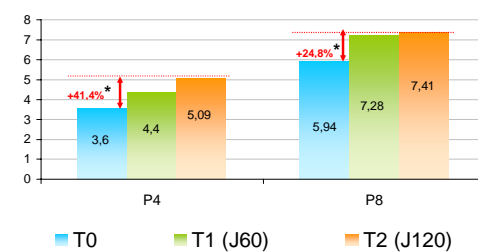


Figure 6 : Study of the distribution of levels of grey

*Statistically significant difference

SURFACE INDEX

The surface index (corresponding to healthy skin that has not been affected by melasma) shows a statistically significant increase for the 4 test zones and for the 2 levels of posterisation between T0 and T2 (+ 39% at posterisation 4 and +22.2% at posterisation 8). This means that the relative surface of pigmented zones of the melasma decreased significantly by the end of the study.

SAFETY

The cream did not lead to tightness, tingling or burning. Tolerance at T1 and T2 was good in 15 individuals and good to average in 4 individuals. No allergic reaction has been noted.

Conclusion

This new depigmenting cream, containing PKC and PKA inhibitors, has a significant impact on melasma on skins of phototypes IV to VI. It has a rapid onset of action (60 days) with ongoing improvement till 120 days. It enabled the melasma of all of the individuals included to be lightened clinically: simplified MASI -1/3 (one third) at T1 and -1/2 (one half) at T2; complexion

improved from 48 to 87% at T1 and T2.

These statistically significant results were confirmed by colorimetric methods, image analysis (decrease of the intensity of the colour and of the relative surface of the pigmented zone). Finally, it had a positive impact on the quality of life of the women afflicted as soon as D60.