ORIGINAL ARTICLE

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Reverse skin aging signs by red light photobiomodulation

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Abstract

Background: Photobiomodulation is a process by which the absorption of red light energy produces a series of physiological effects at the cellular level such as the enhancement of mitochondrial Adenosine Triphosphate (ATP) production, cell signaling and growth factor synthesis, and the reduction of oxidative stress. Light emitting diodes (LEDs) photobiomodulation is an increasingly popular therapy for treating skin problems, especially for reversing the signs of skin aging.

Objective: The objective of this study is to demonstrate the effectiveness of a photobiomodulation treatment using red LEDs on the facial skin at a rate of two sessions per week for 3 months. The LED mask used is the Skin Light Dior x Lucibel mask diffusing a cold red light with a wavelength of 630 ± 10 nm and a power of 15.6 J/cm² for a duration of 12 min.

Method: In order to demonstrate the effectiveness of the mask in reversing the signs of skin aging, a clinical study was conducted on 20 healthy Caucasian women: the antiwrinkle effect by measuring the depth of the crow's feet wrinkle, the relaxation of the oval of the face by clinical scoring, the firmness and elasticity of the skin by cutometric measurement, the density of the dermis by ultrasound analysis, the smoothness of the skin by measuring the roughness at the cheek, the homogeneity of the complexion by chromametric measurement, the diameter of the pores by macrophotographs and finally the sebo-regulating effect by measurement of the rate of sebum and quantification of the number of pores containing porphyrin in the subjects presenting a mixed to oily skin. The satisfaction of the volunteers was also evaluated at the end of the study via a self-questionnaire.

Results: The efficacy results measured after 1, 2, and 3 months of use are progressive and confirm the interest of LED photobiomodulation to reverse the visible signs of skin aging.

All the volunteers observed an overall improvement in skin quality.

Conclusion: All the results observed confirm the interest of using photobiomodulation to reverse the visible signs of aging. These results last for up to 1 month after stopping the use of the mask, which is a sign of lasting structural and functional rejuvenation of the skin.

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KEYWORDS

led, low-level laser (light) therapy, photobiomodulation, reverse skin aging

1 | INTRODUCTION

The study of skin aging allows us to identify the key mechanisms of skin functions and structure. It is possible to measure the evolution of these mechanisms according to genetic factors (chronological age) but also environmental factors (nutrition, lifestyle, sport, UV exposure) allowing to define a biological age of the skin. This evolution translates into the appearance of visible clinical signs on the face, responsible for the increase in the perceived age of an individual. The main signs of age are the appearance of wrinkles and fine lines, the decrease in firmness, the loss of density.

In order to reverse the visible signs of skin aging, the use of Low-Level Laser Therapy (LLLT) is becoming more and more common and numerous clinical studies demonstrate its effectiveness. This type of nonablative therapy is based on the principle of photobiomodulation, a cascade of cellular responses induced by low-energy lasers or light emitting diodes (LEDs) in a specific wavelength (400-1100 nm).¹

Photobiomodulation will act through different mechanisms on the skin such as nonvisual opsins, direct activation of Transforming Growth factor $\beta 1^2$ but also activation of cytochrome C oxidase. Indeed, it has been shown that, in the skin, one of the pathways of aging³ was mitochondrial dysfunction and that photobiomodulation by red light, activates cytochrome c oxidase,⁴ which increases mitochondrial production of ATP, which in turn enhances the metabolic activity of the cell.^{5,6} Simultaneously, regulation of the reduction/oxidation (redox) state of the intracellular environment promotes the expression of genes associated with tissue regeneration and repair.⁷

The objective of this study is to demonstrate the effectiveness of a mask using red LEDs, whose characteristics are extremely well defined, on reversing the signs of aging as early as 1 month after its use.

2 | LED (Light Emitting Diode) and the skin

The light used in low intensity laser therapy can be produced by LEDs which are monochromatic lights that can be red, blue, yellow or green depending on the wavelength used (Figure 1).

Light emitting diodes (LEDs) are defined by irradiation parameters and irradiation time. The energy (J) or energy density (J/cm²) is the descriptor of the irradiation time which depends on two components, power, and time.

Energy $(J) = Power (W) \times Time (s).$

Irradiance parameters are defined in intensity or power density.

Light scattering in tissue is higher at shorter wavelengths and, in addition, water strongly absorbs infrared light at wavelengths longer than 1100 nm.

Therefore, the use of LLLT makes almost exclusively red and near infrared light (600–1100 nm). $^7\,$

Photobiomodulation is characterized by its ability to induce photobiological processes in cells at the level of mitochondria. Indeed, they play an important role in the production and generation of energy and metabolism by converting food molecules into energy in the form of ATP through oxidative phosphorylation.

The mechanism of LLLT at the cellular level has been attributed to the absorption of visible and near-infrared monochromatic radiation by components of the cellular respiratory chain, resulting in increased ATP synthesis, increased RNA and protein synthesis, and increases in oxygen consumption, membrane potential, and NADH and ATP synthesis.⁷

Once the cellular mechanisms have been reactivated, a few days are necessary for the photobiomodulation to be at its maximum efficiency. It is therefore not useful to do a daily session but rather to space out the sessions by 72 h. The Arndt-Schulz law is often cited as an appropriate model to describe the dose effects of LLLT.⁸ Indeed the "stimulus" increasing with the duration of irradiation or the increase of irradiation allows to apply an energy but if this one is too weak, there will be no response (because the minimum threshold was not reached) and if the energy is too important, the stimulation disappears and is replaced by a bioinhibition.⁸

In this study we will focus on the effects of red light, which is known for its rejuvenating efficacy, although other colors also have skin benefits. Unlike other colors, red LED light (600–700 nm) reaches

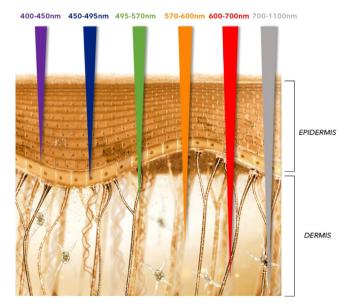


FIGURE 1 Light penetration level according to its wavelength.

Irradiance = Power (W)/Area (cm^2).

TABLE 1 Technical comparison of the various light emitting diode (LED) masks on the market today.

Name	Symbol	Unit	beauty mask*	* body*	mask*	Lucibel*	
Emission Surface	LES	cm ²	558	378	252	337	
Total optical power	Popt	W	0,2	0,5	0,1	10,1	
Average irradiance	Emoy	mW/cm ²	0,3	1,2	0,03	21,7	
Processing time	t	min	30	10	20	12	
Dose	D	J/cm ²	0,6	0,7	0,04	15,6	
Electric power	Pelec	W	5,6	n/a	5	40	
Number of LEDs	N°led	/	192	56	17	40	
Pelec/Nled	/	W	0,029	n/a	0,29	0,97	
Wave length	λ	nm	630	630	630	635	
Treatment lenght equivalent efficiency	/	/	14H	8.5H	24H	12 IN	

*Technical data Lucibel.

the dermis⁹ and is mainly used for its antiaging action and its ability to accelerate healing. In addition to reducing wrinkles, it stimulates fibroblasts and thus increases the production of collagen and elastin.⁹

Thanks to its ability to stimulate cellular metabolisms, confirmed in recent years by numerous studies,¹⁰⁻¹⁴ photobiomodulation has now spread to many fields of medicine such as endocrinology, neurosurgery, dermatology and dentistry.¹⁵

3 | MATERIAL AND METHODS

3.1 | Tested device

The tested mask is the Skin Light Dior × Lucibel mask. Lucibel is a French company expert in new generation lighting products and solutions based on LED technology.

This mask emits a red light with a wavelength of 630 ± 10 nm and a power of 15 Joules*/cm² in accordance with the scientific literature to provide maximum efficiency. This choice was also guided by the resistance limit of the diodes, that is, 15.6 Joules/cm² with a power density of 21.7 mW per cm². Lucibel's research allowed to choose only the red light rather than the combination of red light and infrared light, to minimize the risks for a home device. Indeed, the risk of pigmentation especially on dark skins. The skin is a sensor and perceives separately the frequencies of red and infrared. When these two wavelengths are combined, the near infrared can develop heat effects which have not been observed when using red wavelengths alone.^{16,17}

It is currently one of the most powerful on the market (Table 1) and can define a protocol on the skin for a duration of 12 min only, without any risk to health. This duration of 12 min has been defined on the basis of the power and quality of LEDs used (High Quality LEDs).

Indeed, the power density is related to the results of skin efficiency rather than considering the overall fluence delivered and has given rise to a patent.¹⁸ Indeed, if we define a remarkable line called meridian from the forehead to the chin and a plurality of remarkable lines

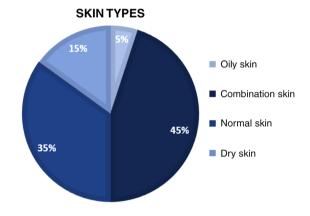


FIGURE 2 Distribution of skin types in the panel.

called parallel lines extending between each side of the face substantially transversely to the meridian line, the light points of the mask are arranged essentially along the parallel lines in order to produce a spatial distribution of the energetic illumination of the face with a maximum light power density along these lines. This power density allowed us to set the time to 12 min.

Thanks to the mapping, the use of red light in photobiomodulation allows the inclusion of phototypes 5 and 6 without risk.

*The joules correspond to the fluence (light power), that is, the quantity of energy received by the cell in the illuminated area during a given time.

3.1.1 | Subjects

The study involved 20 healthy volunteers (15 women and five men), between 45 and 70 years of age (average age: 55.6 ± 7.39 years) with signs of skin aging (wrinkles, lack of tone, roughness of the skin, etc.).

The distribution of the volunteers' skin type is presented in the graph below (Figure 2):

All participants were informed of the purpose of the study, signed an informed consent form including image rights upon arrival, and

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received compensation for their participation at the end of the test.

3.1.2 | Experimental acquisition device

The research center that conducted the study is a service company specialized in clinical evaluation in dermato-cosmetology in France, as well as in histological, biochemical, and biological research and evaluation. The clinical team was trained to handle all the tools provided with a dedicated operator for the whole study and for the same tool.

<u>LifeViz micro photographs:</u> The evaluation of wrinkles and skin texture is performed using LifeViz micro photographs. The analysis of wrinkles is performed on the deepest crow's feet wrinkle and the analysis of roughness on the upper part of the cheek.

<u>Atlas of cutaneous aging¹⁹</u> The clinical evaluation of the sagging of the oval of the face is performed by the dermatologist using the Atlas of cutaneous aging 6-grade scale (0 being no sagging and 5 a very strong sagging).

<u>Cutometer</u>: The firmness and elasticity of the skin were measured using the Cutometer, a measuring instrument that creates a negative pressure (suction) that deforms the skin, making it possible to evaluate its biomechanical properties.

<u>Ultrasound</u>: Ultrasound was performed on the right cheek with a 12.1 mm 2D 20 MHz narrow-focus probe. The image taking and the analysis of the dermis density are performed with the Advanced Control software.

<u>Macrophotographs with the Proscope :</u> The diameter of the pores is visualized using macrophotographs taken with the PROSCOPE (x30) at the level of the cheek in contact with the wings of the nose.

<u>Chromameter CR400:</u> The homogeneity of the complexion was evaluated with the help of the Chromameter CR400 allowing the measurement of the parameter L* which represents the luminosity of the complexion on 2 zones (internal part and external part of the cheek). A decrease in the difference between the two areas shows an increase in the homogeneity of the complexion.

<u>Skin Diagnostic SD 207</u>: The measurement of the sebum level is performed with the Skin Diagnostic SM 815 sebum meter on the cheek in contact with the nose wing. This measurement is carried out only for subjects with mixed to oily skin (10 volunteers).

<u>Visiopor</u>: The quantity of porphyrins contained in the pores is visualized by taking macrophotographs at the level of the left cheek in contact with the wing of the nose using the VISIOPOR PP 34 using an ultra violet light. This measurement is performed only for subjects with mixed to oily skin (10 volunteers).

3.2 Protocol

The Skin Light Dior \times Lucibel mask is given to the volunteers at D0 so that they can perform a 12-min pre-programmed LED session on the face twice a week for 3 months. These sessions must be spaced 72 h apart in order to respect the cellular energy digestion time and have an

optimal delay effect already proven in photobiomodulation. Volunteers are asked to wear the protective eyewear provided and to keep their face clean and make-up free for each session.

Throughout the study, the subjects keep their usual day and night care, cleansing products and make-up products.

Efficacy measurements are performed, under dermatological control, every month for 3 months (D0, D28, D56, D84).

The same efficacy measurements were performed 14 and 28 days after stopping the use of the mask and compared to the values obtained at D84 in order to evaluate the persistence, over time, of the antiaging effect.

Finally, the satisfaction of the volunteers was evaluated at the end of the study via a self-questionnaire.

3.2.1 | Statistics analysis

The two-tailed Student's *t* test for paired data is performed if the data follow a Normal distribution (verified by the Shapiro Wilk test). Otherwise, the non-parametric Wilcoxon test is performed. For all statistical tests, an alpha risk of 5% is used (significance < 0).

3.2.2 | Ethics disposition

Regulatory Procedures

This study with an independent ethics committee and was conducted in accordance with:

- 1. Good clinical practices (PPC, July 1996)
- 2. the law of 20 December 1988 (n°2004-806 of 9 August 2004)
- 3. the declaration of Helsinki (1964)

The volunteers

Recruitment was carried out from the volunteer panel of an independent Contract Research Organization (CRO). The identity of each subject participating in the study was kept confidential through the use of an identification number.

A consent to participate was dated and signed by the subject and the investigator in duplicate. A copy was kept by the subject.

The investigator has agreed to comply with the protocol. Any modification must be discussed in advance between the investigator and the sponsor. All original study data are kept for 10 years by the CRO.

Each volunteer was given a Skin Light Dior \times Lucibel mask to carry out the study at home and returned it to the investigator; they were also paid for their participation in the study.

4 | RESULTS

The clinical study shows excellent dermatological tolerance and antiaging effectiveness of the Skin Light Dior \times Lucibel mask after 1, 2, and 3 months of use.

From the first month of use (D28), a significant improvement in the following parameters was observed

1. 15.6% decrease in the depth of crow's feet wrinkle,

Depth of the crow's feet wrinkle (mm)

- 2. Decrease of 5.4% of the clinical score of slackening of the oval of the face and 13.6% of the RO value translating a firming effect,
- 3. 26.4% increase in dermal density,
- 4. 6.8% decrease in cheek roughness and 28.5% decrease in pore diameter, indicating a smoothing effect,

4.1 | Crow's feet wrinkle

Mean (n=20)

0,1

0,08

0,06

0,02

0

Wrinkle depth (mm)

A significant decrease in the depth of the crow's feet wrinkle of 15.6% was observed after 28 days of mask use, 34.7% after 56 days and 38.3% after 84 days.

D0

 0.077 ± 0.03

D28

 0.065 ± 0.02

Figure 3 shows the reduction in crow's-feet wrinkling observed in subject number 11 after 84 days.

0,04

-38.3%

D84

-34.7%

D56

*Significant according to Student's T test with p < 0.05%.

D28

Evolution of the depth of the crow's feet wrinkle

-15.6%

Sagging of the oval of the face 4.2

DO

A significant reduction in sagging of the facial oval of 5.4% is observed after 28 days of use of the mask, 14.7% after 56 days and 24.8% after 84 days.

Sagging of the oval of the face (Bazin score)			е	D0		D28	C	056	D84		
Mean (n=20)					3.23 ± 0.73	3.05	5 ± 0.069	2.75	± 0.62	2.43 ± 0.61	
Bazin score	4 3 2 1 0	Evolution of th	*	-14.7%							
		DO	D28	D56	D84						

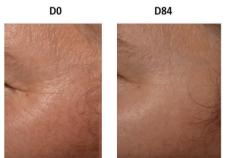
*Significant according to Student's T test with p < 0.05%.

5. 34.9% decrease in the quantity of sebum.

After 2 months of use (D56), a further improvement in the above parameters was noted. A significant increase of 12.5% in skin elasticity and 32.7% in skin tone homogeneity were also observed.

After 3 months of use (D84), all the parameters analyzed were improved compared to the values obtained at D56.

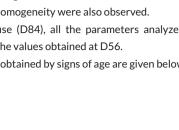
Details of the results obtained by signs of age are given below:



D56

 0.050 ± 0.02

FIGURE 3 Decrease in crow's feet wrinkle observed in subject number 11 after 84 days



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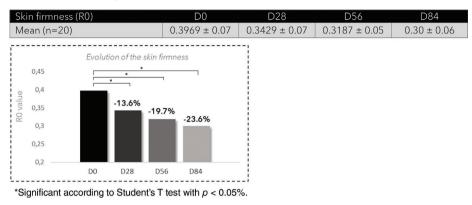
D84

 0.047 ± 0.03



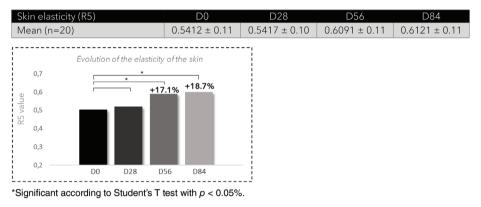
4.3 | Skin firmness

A significant decrease in the RO value of 13.6% was observed after 28 days of mask use, 19.7% after 56 days and 23.6% after 84 days. These decreases reflect a progressive increase in skin firmness.



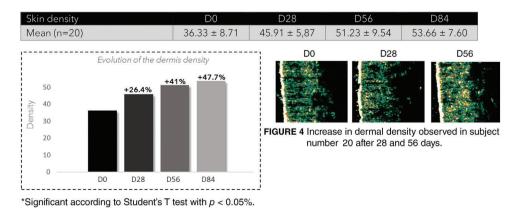
4.4 | Skin elasticity

A significant increase in the R5 value of 17.1% is observed after 56 days of mask use and 18.7% after 84 days.



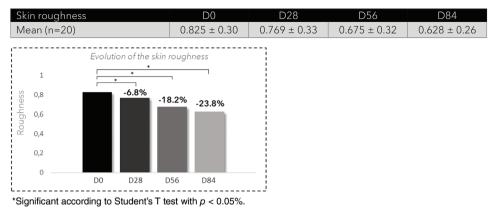
4.5 | Skin density

A significant increase in dermal density of 26.4% was observed after 28 days of mask use, 41% after 56 days and 47.7% after 84 days. Figure 4 shows the increase in dermal density observed in subject number 20 after 28 and 56 days.



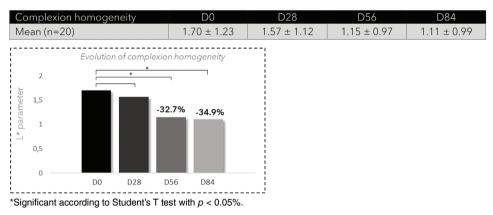
4.6 | Skin roughness

A significant decrease in roughness of 6.8% was observed after 28 days of mask use, 18.2% after 56 days and 23.8% after 84 days. These decreases reflect a progressive increase in skin smoothness.



4.7 | Complexion homogeneity

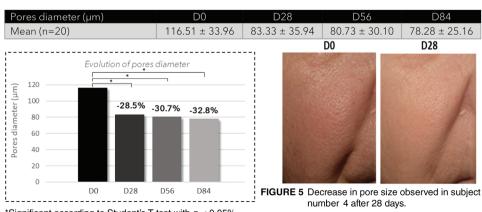
A significant decrease in the L* parameter of 32.7% was observed after 56 days of mask use and 34.9% after 84 days. These decreases reflect a progressive increase in homogeneity.



4.8 | Pores diameter

A significant decrease in pore diameter of 28.5% is observed after 28 days of mask use, 30.7% after 56 days and 32.8% after 84 days. This decrease can be observed by photographic visualization.

Figure 5 shows the reduction in pore size observed in subject number 4 after 28 days.

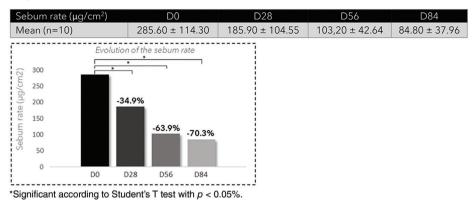


*Significant according to Student's T test with p < 0.05%.



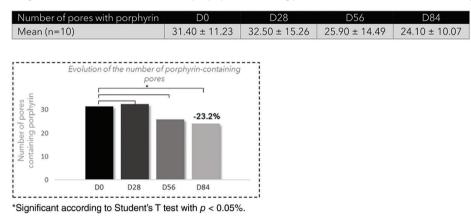
4.9 | Sebum rate

A significant decrease in sebum levels of 34.9% was observed after 28 days of mask use, 63.9% after 56 days and 70.3% after 84 days.



4.10 | Number of pores with porphyrin

A significant decrease in the number of porphyrin-containing pores of 23.2% is observed after 84 days of mask use.



5 | DISCUSSION

It should be noted that the usual use of day-night skincare, cleansing, and makeup products probably remains the best option to not alter and influence skin characteristics, we do not know to what extent the addition of the LED face mask would enhance them. While this may not be feasible at this point, it remains a limitation of the study.

On the other hand, there are no comparative studies to date that allow us to validate that the choice of the power of the light emitting diodes is the most effective. It should be noted, however, that the bibliographic bases give the limit acceptable by the skin cells in terms of power but also of repetition. Indeed, photobiomodulation follows the rules of the dose-dependent biphasic response (Arndt-Schulz curve), a principle that states that there are optimal parameters identified as the appropriate dose of light that provides a therapeutic action on the targeted tissues.⁷ Correct identification of the appropriate dose is not an easy process in photobiomodulation, due to the many parameters through which Light amplification by stimulated emission of radiation (LASERs)/LEDs emit their energy and this leads to a lack of standardized protocols in various clinical applications. However, even without a definitive consensus, there is a large amount of positive clinical evidence that supports the beneficial effects of photobiomodulation in wound healing, tissue repair in particular. The purpose of this publication is to give a first numerical approach of the results that can be obtained by photobiomodulation on the skin.

The results obtained during this clinical study attest to the effectiveness of the use of the Skin Light Dior \times Lucibel mask in reversing skin aging, the signs of which have evolved favorably (see Figure 6).

The satisfaction questionnaire after 2 and 3 months of use reflects this effectiveness: 100% of the volunteers find that the mask significantly improves the overall condition of their skin and 85% of the volunteers felt good after a session.

The analysis of the results obtained separately on the men/women panel follows the same trend. Indeed, despite the small number of men included in the test (five men), the results all point in the same direction after 3 months of using the mask:

- 16.7% decrease in the sagging of the oval of the face,
- 31.3% decrease in the RO value, indicating an increase in skin firmness,

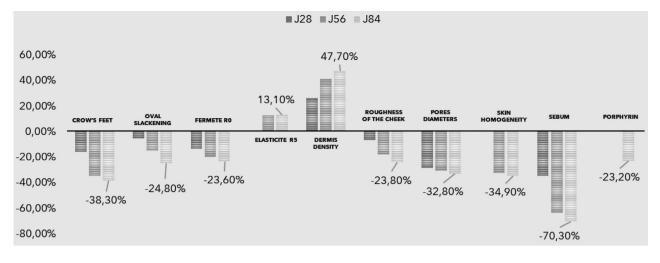


FIGURE 6 Reverse skin aging signs after 28, 56, and 84 day use of the Skin Light Dior × Lucibel mask. *Significant according to Student's T test with *p* < 0.05%.

- 62.1% increase in dermal density,
- 28.1% decrease in pore diameter,
- 62.6% decrease in the amount of sebum.

Measurements taken 14 and 28 days after stopping the use of the Skin Light Dior × Lucibel mask confirm that the reversal of the signs of aging is long-lasting and profound. Indeed, the results on crow's feet wrinkles, the sagging of the oval of the face, the firmness, the density, the roughness of the skin, the diameter of the pores, the homogeneity of the complexion, the rate of sebum, and the quantity of porphyrin remain at the same level as those obtained after 3 months of use of the mask (with no significant difference), demonstrating the remanence of effectiveness.

6 CONCLUSION

This clinical study confirms the interest of photobiomodulation in the treatment of the signs of skin aging. From the very first sessions, whatever the age of the person, the visible effects of reversing the signs of aging are not only observable but also measurable.

During a photobiomodulation therapy, it is important to consider the power and the time of use. Indeed, when the sessions are too long, or when the device does not allow for the treatment of a large surface, compliance decreases. The Skin Light Dior x Lucibel mask has the advantage of treating the entire surface of the face in only 12 min. This is a short time during which cellular metabolisms are stimulated and skin repair and regeneration mechanisms are accelerated.

CONFLICT OF INTEREST STATEMENT

VC, ML, MP, and CG have no conflict of interest. CG is CEO of Lucibel Group and MP is a consultant for Lucibel Group.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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How to cite this article: Couturaud V, Le Fur M, Pelletier M, Granotier F. Reverse skin aging signs by red light photobiomodulation. *Skin Res Technol*. 2023;29:e13391. https://doi.org/10.1111/srt.13391