NEGATIVE EFFECT OF BLUE LIGHT AND POTENTIAL IMPACTS ON THE DERMIS

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INTRODUCTION

Premature skin aging evidenced by a rough skin texture and wrinkles is well known to be driven by external factors, mainly by sunlight and in particular UV radiation including UVB (280-320 nm) and UVA (320-400 nm). Recent advances highlighted the potent role of visible light, and especially blue light, in causing skin damage and premature aging.

In the first part we demonstrated the negative effect of blue light on skin biopsies and in the second part we evaluated the benefits of a botanical extract to bring a broad protection from sunlight, including UVB and the short wavelength of the visible light.

HYPOTHESIS

Blue light is a high energy visible (HEV) light with a wavelength ranging between 400 nm to 500 nm (Figure 1). Depending on the wavelength and dose applied, blue light influences physiological responses, and impacts health (1-2). A recent publication mentions that blue light, especially with a shorter wavelength, may contributes to skin aging similar to UVA (3).

The blue light penetrates deeper into the skin and damages the skin by inducing oxidative stress and production of proteases, including the metalloproteinase 1 (MMP1) which degrade the extracellular matrix, mainly collagens of the dermis (4).

The aim of our study was to evaluate the effect of the blue light on the production of MMP1 in human skin biopsies *in vitro* to evaluate its potential negative impact in the dermis and its implication in skin aging.

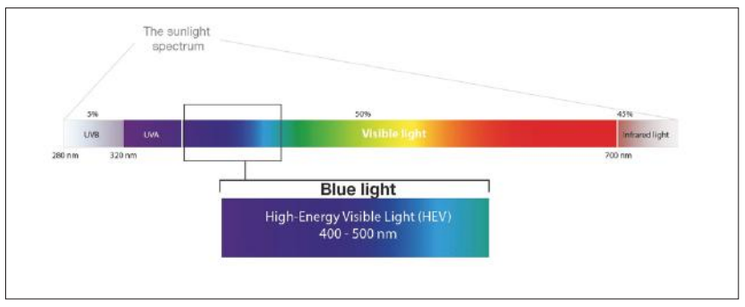

Figure 1: Spectral distribution of solar irradiance in the skin

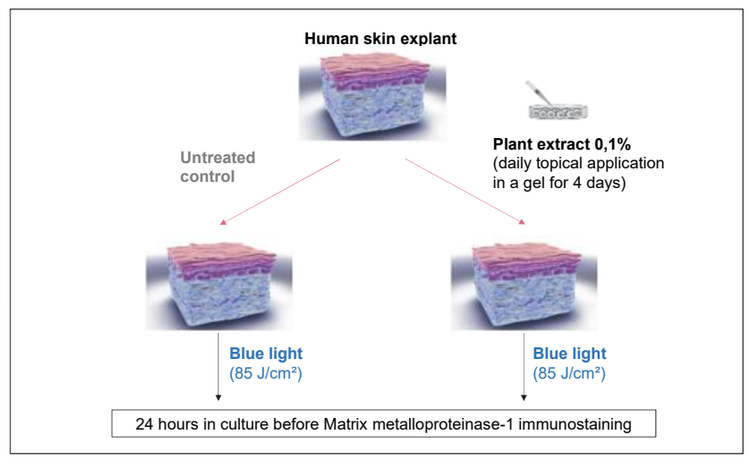

Figure 2: MMP1 protein level in human skin

METHODS

1-Thymine dimers on reconstructed skin

Fibroblasts from an 18yo donor were grown for 4 weeks on collagen based sponge in Green based medium. Keratinocytes from a 24 yo donor were then seeded and cultured for 7 days in a DMEM/Ham's medium with specific nutrients before air exposure for 13 additional days. Reconstructed skins were systemically treated, or not, with the plant extract at 0.03% for 4 hours before being irradiated, or not, in PBS by UVB at 50mJ/cm². Thymine dimers were quantified 4 hours post irradiation after immunostaining using Leica confocal microscope and Image J software (mouse monoclonal antibody clone H3 (Sigma), Alexa 488-secondary antibody (Invitrogen), counterstaining by Evans Blue, (Biomerieux)).

2-DNA repair: NER gene expression

Keratinocytes (37 to 47yo donors) were cultivated on type I collagen for 3 days in DMEM with10% FCS and treated or not (control) with the plant extract at 0.001% for 24 hours. The levels of expression of *XPC (*Xeroderma Pigmentosum, complementation group C), *DDB2* (Damage specific DNA Binding protein 2) and *POLH* (DNA Polymerase Eta) gene, which belong to the Nucleotide Excision Repair pathway (NER), were quantified by qRTPCR.

3-Blue light effect on MMP1

Skin samples obtained from abdominal plastic surgery (women 32 to 51yo) were topically treated, or not, during 4 days by 2 mg/cm² of carboxymethyl cellulose gel with 0.1% plant extract. Skin samples were then irradiated or not in HBSS with blue light at 85 J/cm² (400-500nm, peak at 455nm) using a Solarbox, then cultured for 1 additional day in define medium.

MMP1 protein expression was evaluated after immunostaining (formalin fixation, MMP1 mouse monoclonal clone 36665 revealed by Vector VIP Peroxidase HRP kit), light microscope observation and image analysis (Cell^D imaging systems). Figure 2.

RESULTS

1- Thymine dimers in reconstructed skins

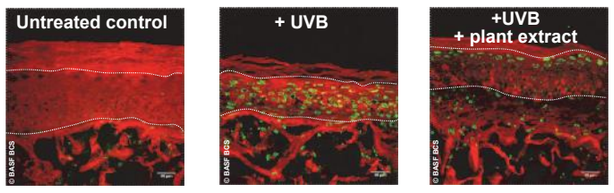

Figure 3: Visualization of thymine dimers (green) - Scale 40µM

After UVB exposure:
- Increase of thymine dimers

With the plant extract:
- Decrease of the number and intensity of the gren staining, mainly in the deeper layers of the epidermis, indicating a protection against UVB induced damage.

2- DNA repair mechanisms in keratinocytes

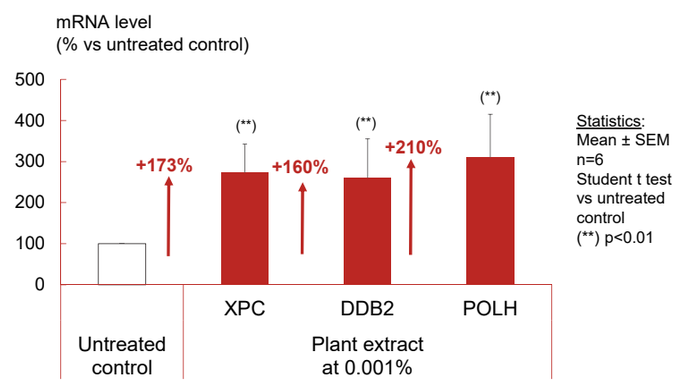

Figure 4: Expression level of genes from the NER pathway in human keratinocytes

The gene expression of 3 genes involved in DNA repair significantly increased with the plant extract:
- + 173% for *XPC*
- + 160% *for DDB2*
- + 210% for *POLH*

3- Blue light effect on MMP1

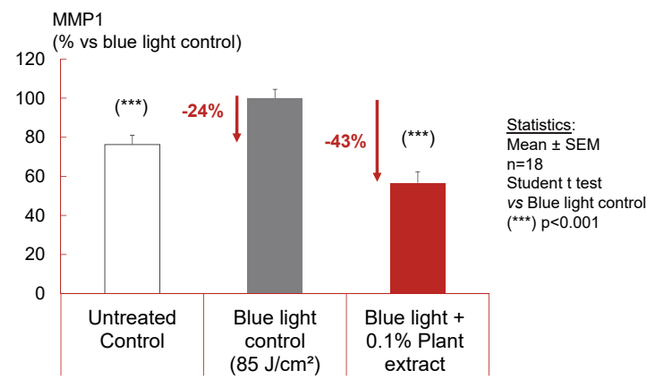

Figure 5 : Effect of blue light on Metalloproteinase-I in skin biopsies.

The plant extract decreased the Blue light induced metalloproteinase-1 that is involved in the degradation of the extracellular matrix of the dermis.

CONCLUSION

As blue light is the most energetic part of visible light and can penetrate deeply into the skin, it is important to take in consideration its impact in skin premature aging and to offer an efficient broad-spectrum solution to protect the skin from the epidermis to the dermis.

We evidenced that the Blue light induced MMP1 increase that could be prevented by a *Cistus monspeliensis* aerial parts extract (titrated in Myricetin glycosides), that could also prevent UVB induced DNA damage and improve the DNA repair mechanisms.

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