

EFFECT OF SUNSCREEN ON PROTOPORPHYRIN IX PHOTOBLEACHING IN *EX VIVO* HUMAN SKIN

K. Sevin, A. Gaborit, G. Bouvier, P. Comby, O. Duffy-Roger, D. Kerob, B. Ruty, H. Osman-Ponchet

Metabolism & Pharmacokinetics Unit, Preclinical development, GALDERMA R&D, Sophia-Antipolis, France

BACKGROUND

Metvix[®]-photodynamic therapy (PDT) is a successful treatment for non-melanoma skin cancers. Methyl-aminolevulinate, the active ingredient of Metvix[®], is a prodrug that is metabolized to protoporphyrin IX (PpIX) which accumulates in the skin lesions. Light activation of accumulated porphyrins leads to a photochemical reaction and thereby phototoxicity of target cells. Pain related to illumination during conventional Metvix[®]-PDT is a severe side effect. PDT using daylight exposure is now used to reduce pain and subjects are advised to protect the non-treated areas with sunscreen. The choice of sunscreen is particularly important as physical filters within sunscreen (such as Titanium or zinc oxide) may inhibit the absorption of visible light which is necessary for PpIX activation. The main objective of this work was to investigate the effect of Actinica[®] Lotion on PpIX photoactivation in *ex vivo* human skin.

METHODS

Frozen excised human skin samples were treated with PpIX solution in DMSO (100 µg/cm²) for 1 hour at 37°C, 5% CO₂ (Figure 1). Due to its high molecular weight, PpIX penetration was facilitated by pretreating skin samples with a microneedle roller device (Figure 2). Skin samples were then treated with Actinica[®] Lotion (SPF 50+) and exposed to solar simulator for 1 hour (Figures 3 and 4A). Skin samples not treated with Actinica[®] Lotion and not exposed to solar simulator were used as controls. PpIX concentrations in total skin were measured by HPLC with fluorescence detection (Figure 4B). Statistical analysis was performed using two-way ANOVA test. A *p* value < 0.05 was considered as statistically significant. Each condition was performed in triplicate on 3 different donors.

Figure 1: Skin samples treated with PpIX solution

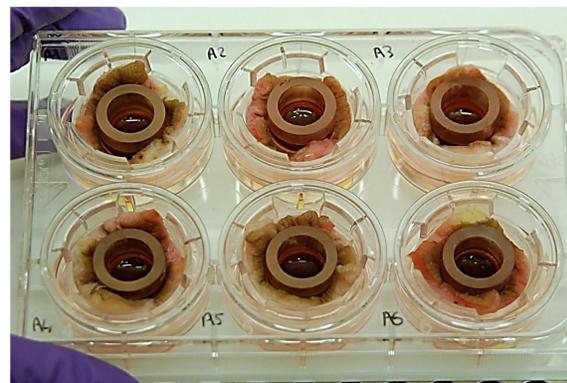
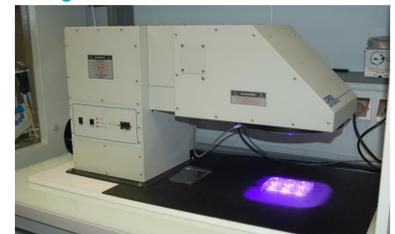


Figure 2: Microneedle roller device



Figure 3: Solar simulator



RESULTS

Figure 4: A- Spectral output curve of solar simulator. B- Chemical structure and absorption spectra of PpIX

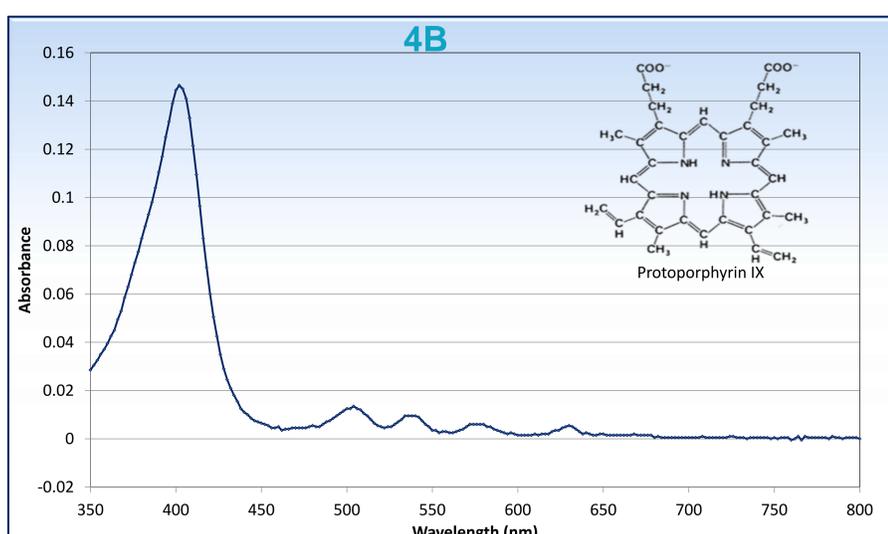
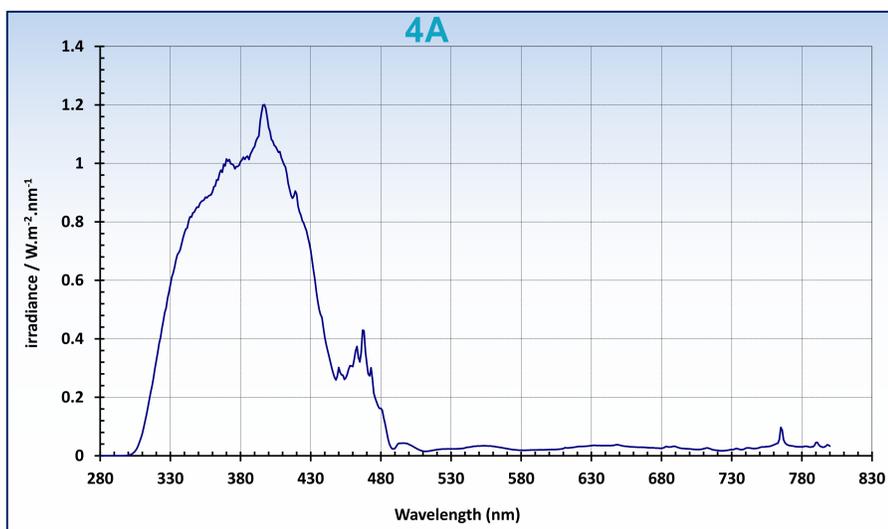
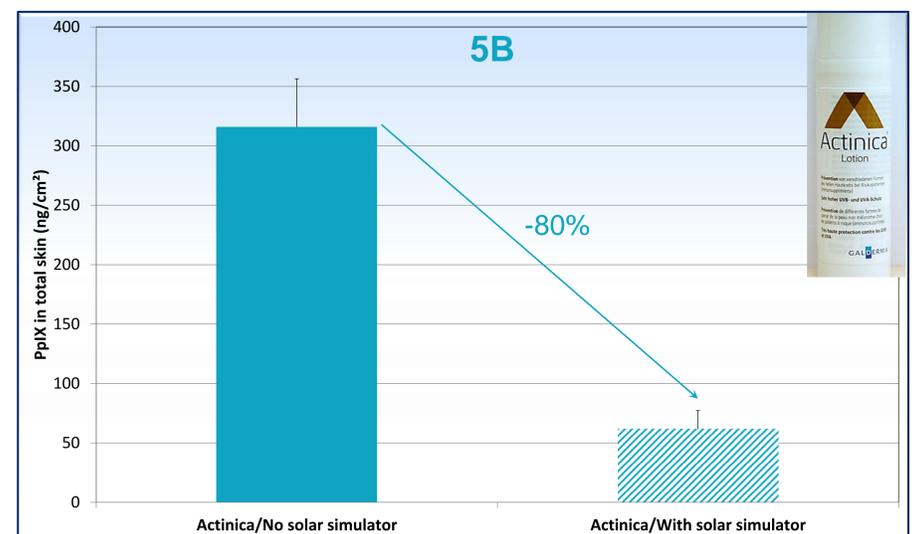
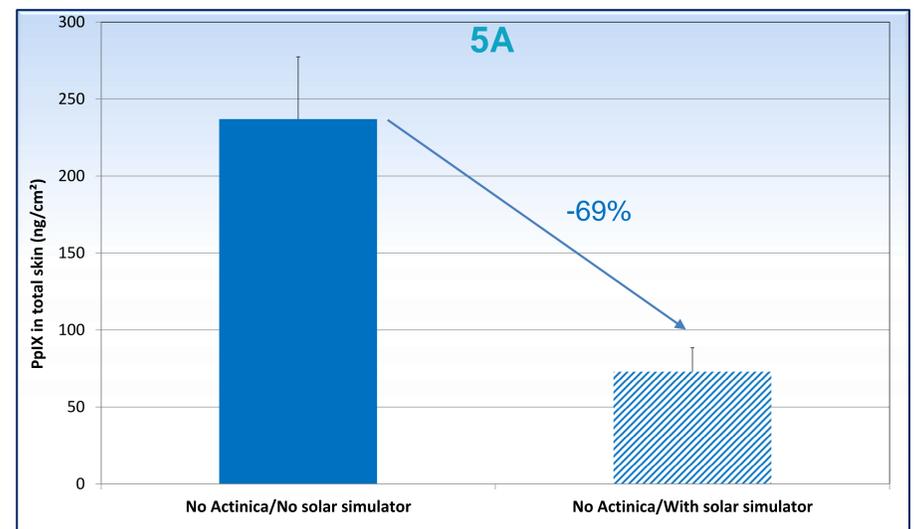


Figure 5: Concentrations (ng/cm²) of PpIX in total skin. A- Without Actinica[®] Lotion. B- With Actinica[®] Lotion. Data represent mean +/- SEM (N = 9)



Effect of solar simulator exposures on PpIX photoactivation were similar without (Figure 5A) and with pre-treatment (Figure 5B) with Actinica[®] Lotion, representing decreases of PpIX content in total skin by 69% and 80%, respectively. This indicates that Actinica[®] Lotion had no significant effect on PpIX photoactivation.

CONCLUSION

The results showed that Actinica[®] Lotion had no effect on PpIX photoactivation in *ex vivo* human skin. Therefore, Actinica[®] Lotion is unlikely to modify the clinical efficacy profile of Metvix in daylight photodynamic therapy.