

EFFECT OF ACTINICA® LOTION SUNSCREEN ON METVIX ABSORPTION IN EX VIVO HUMAN SKIN

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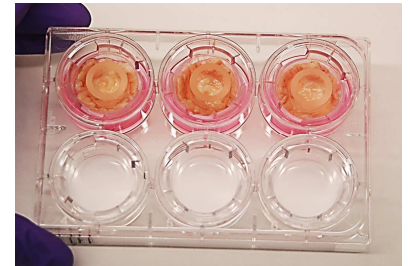
BACKGROUND

Metvix® cream contains methyl aminolevulinate (MAL). Conventional Metvix® photodynamic therapy (cPDT) has proved efficacious for the treatment of certain types of actinic keratoses and basal cell carcinomas. However, pain related to illumination during conventional Metvix®-PDT is a severe side effect. Replacing conventional PDT by natural daylight PDT may represent a new strategy to reduce pain related to illumination. During exposure to daylight (DL), subjects are advised to utilize a sunscreen on treated and non-treated areas. However, sunscreen may modify skin absorption of MAL, and therefore impact the efficacy and safety of Metvix. The main objective of this work was to evaluate the interaction between Actinica® Lotion sunscreen and Metvix by evaluating the effect of sunscreen on MAL absorption in ex vivo human skin.

METHODS

Human skin samples from three different donors maintained in organoculture on Transwell® inserts were first treated with sunscreen (Actinica® Lotion SPF 50+; 2 µL/cm²) for 5 minutes or 15 minutes according to the group. Afterwards, skin samples were treated with Metvix® cream containing [¹⁴C]-MAL (100 mg/cm²) for 2.5 hours. Skin samples treated with Metvix® cream only were used as control. Incubations were performed in cell incubator set at 37°C and 5% CO₂, under gentle shaking.

At the end of the incubation period, excess of formulation was removed and radioactivity related to [¹⁴C]-MAL was measured by liquid scintillation counting in skin, receptor liquid, formulation excess and washing samples. Each condition was performed in triplicate.



RESULTS

Figure 1: Chemical structure of [¹⁴C]-MAL and Mass balance of [¹⁴C]-MAL in the three different treatment groups

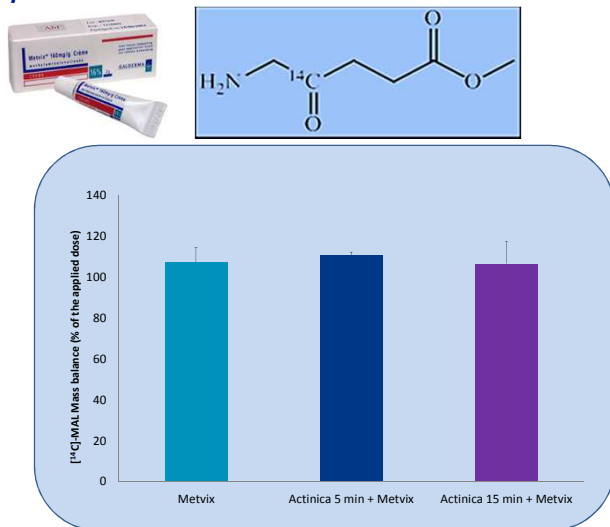
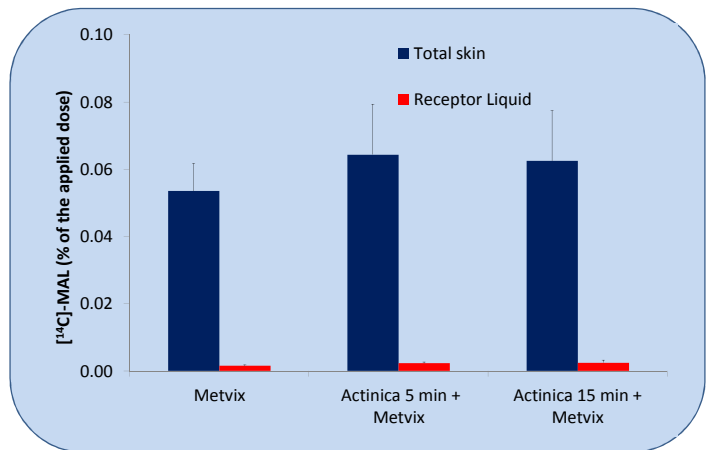


Figure 2: Absorption and distribution of [¹⁴C]-MAL in ex vivo human skin expressed in % of the applied dose
Data represent mean +/- SEM of three donors in triplicate (N = 9)



DISCUSSION

- Mean mass balance values ranged between 107% and 111% in all skin samples (N = 27).
- After 2.5 hours treatment, the mean absorbed dose of [¹⁴C]-MAL in the receptor liquid represented 0.002% of the applied dose in all three treatment groups
- After 2.5 hours treatment, the mean dose of [¹⁴C]-MAL penetrated into the total skin represented 0.05% - 0.06% of the applied dose in all three groups and was more than 25 times the absorbed dose.
- Five or fifteen minutes pretreatment with Actinica® Lotion had no statistically significant effect on [¹⁴C]-MAL skin absorption or distribution.

CONCLUSION

No statistically significant effect of Actinica® Lotion sunscreen was seen on [¹⁴C]-MAL absorption or distribution in ex vivo human skin. This indicates that there was no significant interaction between the sunscreen and Metvix in these in vitro conditions. Therefore, the sunscreen tested (Actinica® Lotion) is unlikely to modify the Metvix efficacy and safety clinical profile.