Cutech
A SYMRISE SCREENING SERVICE

UV INDUCED *EX-VIVO* HUMAN SKIN TANNING MODEL

Cutech, now part of the Symrise Group, is an Italian biotech company that offers screening services based on unique pre-clinical models for skin and related annexes (hair, sebaceous glands).

We focus on *ex-vivo* human skin models based on a distinctive tissue culture, image analysis and bio-information know-how developed during almost 20 years. Cutech's *ex-vivo* testing systems provide a high predictive value to the *in-vivo* situation. Our models and tests allow to gain in-depth information concerning the efficacy as well as mechanism of action of cosmetic ingredients and finished formulations.
In line with the market needs, we steadily develop new innovative test models and also provide tailor-made services. The Cutech screening services allow a faster approach to clinical trials, thus increasing the speed-to-market.

Cutech offers a comprehensive technology platform based on the following core assets:

- proprietary and validated *ex-vivo* human skin models
- reconstructed skin models
- *in-vitro* primary skin and hair follicle cell cultures
- constantly updated list of cellular and molecular read-out parameters
- proprietary image analysis and bioinformatic technologies
- in-depth know-how of skin, hair and sebaceous gland biology

Our best-in-line screening platform and extensive know-how on evaluating potential actives allow us to rapidly and cost-effectively screen the potential of active ingredients and finished formulations.

Depending on the customer needs, we can also propose customized experimental designs.

Since our foundation in 2002, we have been focusing on *ex-vivo* culture technology as we consider it the most effective alternative to *in-vivo* testing. Following this belief, we have been developing and perfecting protocols for culturing *ex-vivo* skin, hair follicles, sebaceous glands and subcutis.

GROUNDBREAKING NEW UV INDUCED *EX-VIVO* SKIN TANNING MODEL IS NOW AVAILABLE IN OUR LABS TO INVESTIGATE THE POTENTIAL OF ACTIVES, PROTOTYPES OR FINISHED FORMULATIONS IN PREVENTING OR MODULATING THE PIGMENTATION

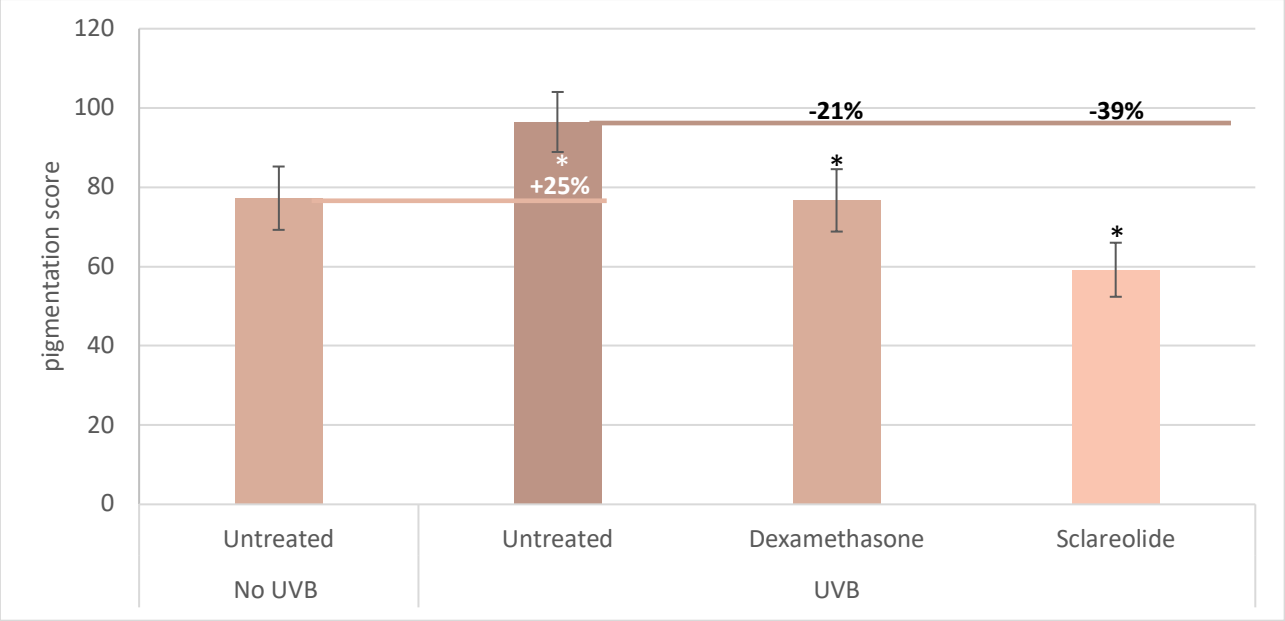
UV radiation induces immediate pigment darkening (IPD) by chemical modification of melanin and possibly spatial redistribution of melanosomes in keratinocytes and melanocytes. UV exposure also leads to delayed tanning (DT) by new synthesis of melanin over several days after UV exposure and persists for weeks (Routaboul et al, Eur J Dermatol, 1999; Maddodi et al., Photochem Photobiol. 2012; Hönigsman. Photodermatol Photoimmunol Photomed, 2002). Despite the high need for a preclinical model to study the modulation of UV induced pigmentation, there is not any available in the market to fulfil this purpose. By taking advantage of our highly evolved technology and competence on ex-vivo skin we have been able to fill this gap by developing a model in which it is possible to induce the increase of skin pigmentation, through repetitive UVB irradiations, and test possible modulators of the tanning effect.

Methodology

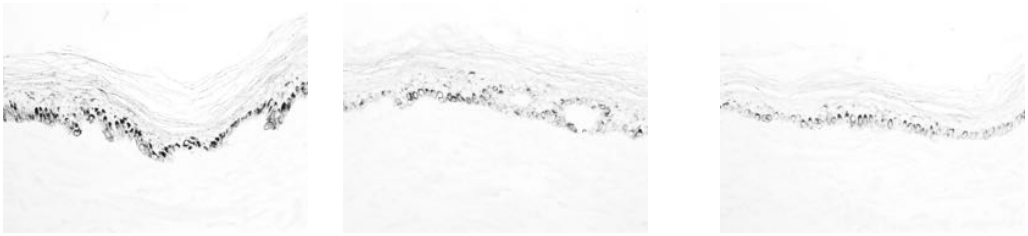
Immediately after having received the skin sample from the clinic, following the selection and the analysis of the skin phototype, skin biopsies are put in culture with specific Cutech culture medium.
Starting from day 1 the skin biopsies are irradiated daily with 75mJ/cm^2. The irradiation is performed with a BIO-SUN system (by Vilber Lourmat ^{TM}). A micro-processor controlled UV irradiation system constantly monitors the UV light emission and stops automatically when the energy received from the skin samples matches the programmed one.
At the end of the experimental phase skin samples are harvested, fixed in formalin, embedded in paraplast and cut at the micro-tome for Fontana-Masson staining. The amount of melanin present in each slide is evaluated by estimating grey intensity and distribution within the sections using dedicated image analysis software.

Results

Fontana-Masson staining – Semi-quantitative analyses on skin cross sections



Cross sections of ex-vivo human skin repeatedly exposed to UVB and treated with different test substances (Fontana-Masson staining)



Untreated –UVB | Dexamethasone - UVB | Sclareolide - UVB

The graphic illustrates the results obtained from a representative experiment. From the image, it can be observed that UVB dose has significantly up-regulated skin pigmentation on *ex-vivo* skin and the selected benchmarks/test compounds (i.e. dexamethasone and sclareolide) have significantly counteracted this activity as expected. Under the graph are shown 3 representative pictures of skin cross-sections irradiated with UVB (75 J/cm^2).

Our ex vivo model has shown to be responding to UVB irradiation by tanning and that this activity can be modulated by effective test samples.

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Cited literature:

N. Maddodi, A. Jayanthy, V. Setaluri. Shining light on skin pigmentation: the darker and the brighter side effects of UV radiation. Photochemistry and Photobiology, Volume 88, Issue5, 2012.

C. Routaboul, A. Denis, A. Vinche. Immediate pigment darkening: description, kinetic and biological function. European Journal of Dermatology, 9(2), 1999.

H. Hönigsman. Erythema and pigmentation. Photodermatology Photoimmunology & Photomedicine, 18, 2002.

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