Givaudan

Management of skin hyperpigmentation through SDF-1 control with *Himanthalia elongata* extract

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Introduction

During ageing, human skin is submitted to different troubles. Among them, hyperpigmentation disorder is well-described and especially the ageing spots which have two different origins. The first is related to chronobiologic ageing that leads to a loss of melanogenesis' control due to cells senescence, resulting in localised hyperpigmentation which is more commonly named senile *lentigo* [1]. The second identified biological pathway related to ageing spots is associated to UV exposure [2–6]. Solar *lentigo* promotes an important increase of oxidised proteins due to a dysregulation of proteasome activity associated with the induction of inflammation and stimulation of melanogenesis [7]. It is also described a lipofuscin accumulation [8]. As a consequence, these pigmented spots are an important concern for cosmetic industry due to anaesthetic aspect. Recently, a new protein has been identified as a key regulator of hyper-pigmentation: the SDF-1 (Stromal cell-derived factor 1) or CXCL12 [9–12]. This protein is expressed by papillary dermal fibroblasts and is involved in the control of pigmentation through the inhibition of cAMP signalling pathway in melanocytes from the basal layer, thus triggering a negative retro-control of MITF transcription. SDF-1 expression is significantly reduced in senescent fibroblasts, but also in UV-exposed tissues, highlighting this protein as a new target to develop an efficient active ingredient against skin hyperpigmentation. In this study, we developed an active ingredient, *Himanthalia elongata* extract (HEX) and evaluated its dark spots fader from SDF-1 expression on skin explant until its clinical efficacy.

Materials & Methods

Ex vivo studies

3 independant Caucasian donors

Senile *lentigo*

- HEX pre-treatment
- H_2O_2-induced senescence
- Treatment renewal
- Repetition for 5 days

Solar *lentigo*

- HEX pre-treatment
- UVA+UVB irradiation (global daily exposure)
- Treatment renewal
- Repetition for 5 days

1 SDF-1 immunostaining → Positive cells scoring

2 Fontana Masson → Skin melanin content quantification

3 Oxidised proteins staining

4 Sudan Black B staining → Lipofuscin accumulation

Clinical studies

3 double-blind, randomised and placebo controlled studies

Caucasian

- 20 volunteers
- From 50 to 75 years
- Pigmented ageing spots on hands
- Twice daily application for 28 days

1 Mexameter® analysis

2 DermaScop® pictures

Asian

- 36 volunteers
- From 45 to 65 years
- Pigmented ageing spots on face
- Twice daily application for 28 days

1 VISIA CR2.0 analysis

African

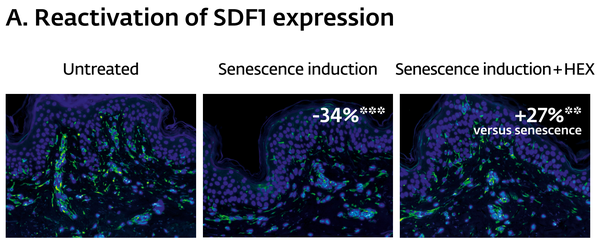
- 43 volunteers
- From 19 to 57 years
- Hyperpigmented spots on face
- Twice daily application for 28 days

1 Mexameter® analysis

Results & Discussion

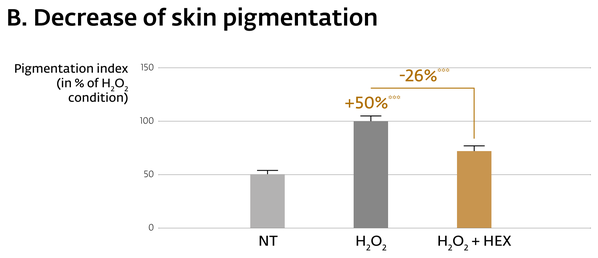
Senile *lentigo*

A. Reactivation of SDF1 expression



HEX reactivates SDF1 expression which was inhibited by senescence induction.

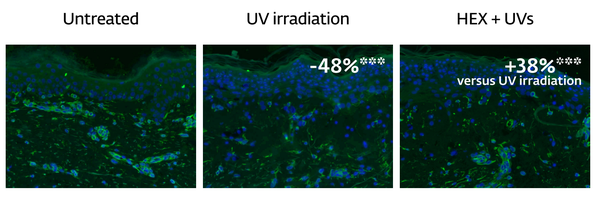
B. Decrease of skin pigmentation



HEX decreases hyperpigmentation induced by senescence.

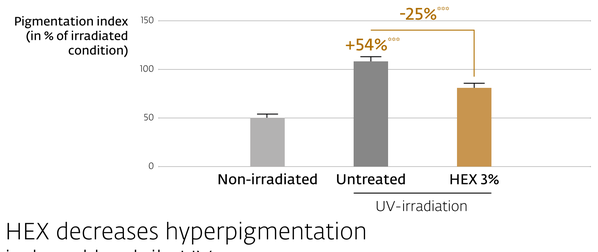
Solar *lentigo*

A. Reactivation of SDF1 expression



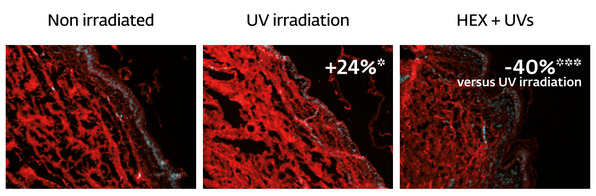
HEX reactivates SDF1 expression which was inhibited by daily UV exposure.

B. Decrease of skin pigmentation



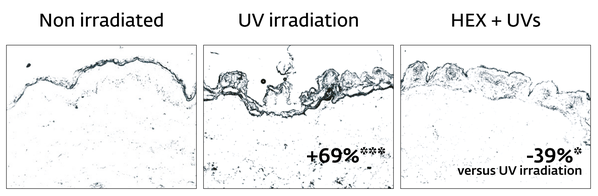
HEX decreases hyperpigmentation induced by daily UV exposure.

C. Protection against protein oxidation



HEX protects skin against protein oxidation induced by daily UV exposure.

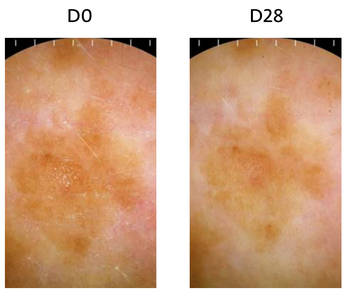
D. Decrease of lipofuscin bodies accumulation



HEX reduces lipofuscin bodies accumulation which is involved in hyperpigmented spots.

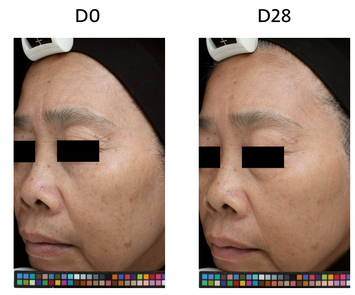
Reduction of hyperpigmented spots

A. Caucasian volunteers



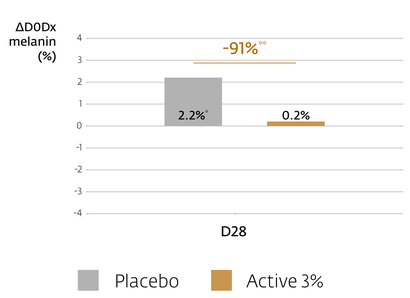
HEX 3%
-12.6%*** versus D0
-103%* versus placebo effect at D28

B. Asian volunteers



HEX 3%
-8.2%*** versus D0
-156%** versus placebo effect at D28

C. African volunteers



-91%** versus placebo effect at D28

Conclusions

Thanks to innovative mimetic models representing the skin disorders leading to hyper pigmented spots apparition on the skin, we were able to highlight *Himanthalia elongata* extract as a powerful candidate to attenuate these anesthetic spots. The development of senile and solar *lentigo* models allowed us explaining the mechanism of action of the active ingredient which restore the control of skin pigmentation by reactivating the expression of a newly identified target regarding pigmentation disorders: SDF1. Clinical studies carried out on almost 100 volunteers from 3 ethnicities achieved to prove the powerful efficacy of *Himanthalia elongata* extract, the new dark spots fader.

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References

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