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When a plant extract delivers well-ageing by epigenetic control as a source of rejuvenation

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Introduction

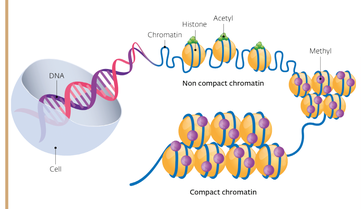
Haberlea Rhodopensis is a part of resurrection plants family with the particularity to be able to regenerate after full desiccation. In the literature, it is described that *H. Rhodopensis* plant regulates its transcriptome activity during desiccation and rehydration phases, therefore modulating its gene expression and as a result it metabolic profile controlling its self-survival leading to resurrection property.

The gene expression is finely regulated by epigenetic mechanisms. Among them, DNA methylation results of Methyl-CpG binding proteins recruitment leading to histone deacetylation and therefore a DNA compaction due to a better affinity with DNA blocking the expression of corresponding genes. During the biological evaluation of our *Rhodopensis harbelea* extract, we evoked the possible biomemtic mechanism which can deliver rejuvenate process through epigenetic control, from plant survival to skin ageing reversal. We demonstrated that some ageing related-pathways are activated due to DNA hypomethylation such as inflammation, excessive fibrosis, apoptosis, inducing skin barrier default. Our active can reverse and restore DNA methylation at the same level than young control showing an drastic improvement of skin elasticity and skin tone and luminosity.

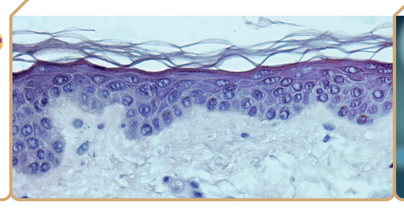
Materials & Methods

In vitro and *ex vivo* evaluation of *Rhodopensis harbelea* extract

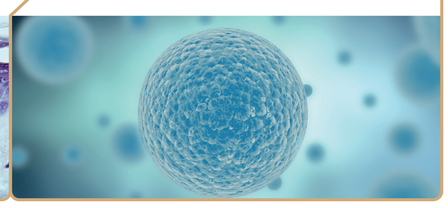
DNA methylation analysis on young, mature and mature treated with our active for 36h.



Proteome rejuvenation analysis using LC-MS/MS after topical treatment on human skin explant for 5 days with our active versus young and mature untreated controls.



Cell rejuvantion analysis by analysing the restoration of β-galactosidase SA activity after 48h of treatment. We then confirmed the rejuvenation effect by analysing the cell morphology which is restored to young one.



Clinical evaluation

Panel description

A double blind clinical evaluation was carried out with 70 women (from 40 to 65 years old, mean age: 51.5 ± 7.5 years), selected for dark skin, lack of elasticity, wrinkles and sagging facial contours. All these volunteers were divided into two groups randomly. 66 subjects completed the entire test, among them, 33 volunteer applied cream 1 (developed by Pechoin containing 1% *H. Rhodopensis* extract) group and 33 others applied cream 2 (developed by Pechoin containing 3% *H. Rhodopensis* extract) group. All of the subjects participating in the study gave their informed consent signed at the beginning of the study.
Volunteers applied cream 1 or cream 2 twice daily for 60 days. All the parameters were measured after D0, D14, D28 and D56.

Wrinkles analysis by Primos 3D on forehead, nasogenian and crow's feet areas after D0, D14, D28, D56

Biomechanical property analysis using cutometer MPA580 conducted after D0, D14, D28, D56

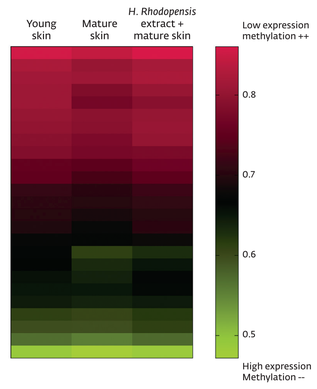
Expert visual evaluation analysed after D0, D14, D28, D56

Illustratve pictures taken by VISIA-CR after D0, D14, D28, D56

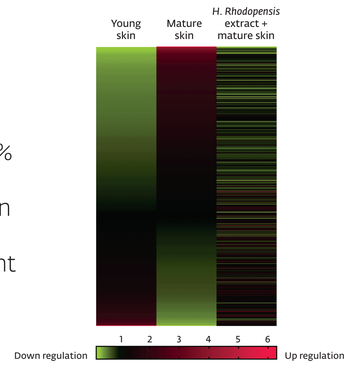
Analysis of skin tone and redness using Chromameter CR400 analysed after D0, D14, D28, D56

Results & Discussion

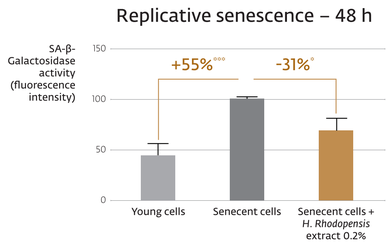
1. Restoration of DNA methylation to young control. Control of ageing through hypomethylation of ageing related-promoters.

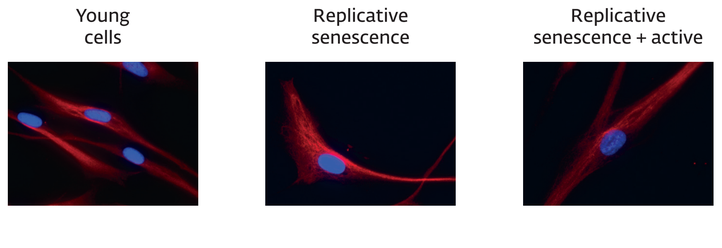


2. Proteome rejuvenation after topical application on skin explant. Improvement of ageing related-proteome by 29% with the extract.
we observed a regulation of protein expression showing an improvement of skin radiance and elasticity.



3. Cell rejuvenation was observed by reducing β galactosidase SA activity and restoration of young cell morphology.

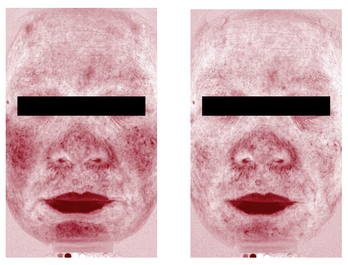




4. Improvement of skin elasticity and radiance were observed on volunteers who have twice daily applied the products at 3% for 56 days. Efficacy has been observed after only 14 days of application showing reduction of redness, better skin luminosity and potent anti-ageing property through reduction of wrinkles and restoration of biomechanical property.

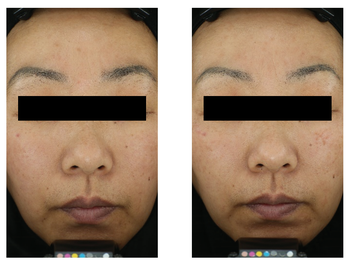
	Skin redness		Skin luminosity		Biomechanical property		Wrinkles reduction		
	a*	Red area ratio	L*	ITA	R2	R7	Nasogenian	Forehead	Crow's feet
D0D14	-2.99%*	-4.88%#	1.32%***	8.25%***	6.99%**	4.78%#	-8.66%***	-6.59%**	-6.94%***
D0D28	-5.52%***	-2.94%	1.23%***	8.25%***	10.16%***	11.84%***	-9.24%***	-5.77%*	-6.80%***
D0D56	-6.36%**	-12.369%***	3.52%***	12.94%***	16.34%***	10.39%***	-8.75%***	-5.51%*	-7.65%***

Reduction of redness



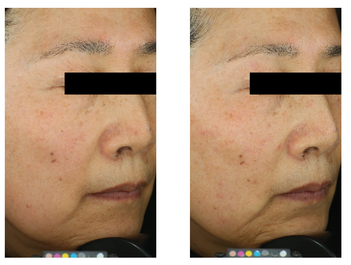
D0 D56

Improvement of skin luminosity



D0 D56

Reduction of face wrinckles



D0 D56

Similar results were obtained with the cream 1 containing 1 % of *rhodopensis harbelea extract*.

Conclusions

On aged fibroblasts, we demonstrated that *H. rhodopensis* at 0.2% applied for 36h induced a significant restoration of methylation degree of ageing impacted-promoters in the same way as young fibroblasts as a proof of rejuvenation activity. The extract significantly inhibited the expression of promoters related to fibrosis, inflammation and apoptosis activities by hyper methylation as an anti-aging mechanism. Finally, we also explored the proteome profile after topical application of *H. rhodopensis* extract at 3% for 5 days on aged skin explants showing a rejuvenation of proteome profile by +29%*. The clinic results further indicated a significant improvement of Skin tone L(+0.77***), ITA(+2.45***); an improvement of crow-feet wrinkles was observed by a decrease of length (-14.9%***)and volume (-8.9%**), and skin elasticity, pore, smoothness were all ameliorated in different degree (28 day data).
Overall these data demonstrated that *H. Rhodopensis* extract ultimately drives clinical benefits of well-ageing and skin radiance, by mimicking rejuvenation mechanisms identified in resurrection plants.

Aknowledgments

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