

Restructuring extra cellular matrix to reduce wrinkles

With age, negative expressions have a tendency to become set as the skin loses its elasticity, and positive expressions lose their structure as the skin starts to sag. While crow's feet are considered as being smile wrinkles, forehead lines on the other hand harden the gaze. Deeper and deeper, nasal furrows with the appearance of circumoral wrinkles indicate bitterness. In young women, high cheekbones and a tapering chin form what is called a triangle of beauty. In older women, forehead lines and nasal furrows delineate an inverse triangle of beauty (Fig. 1).

Natural ageing of the skin is the result of a slow, progressive and genetically determined process. With age, the genes that code for the synthesis of the dermal structural molecules – elastin, collagen and hyaluronic acid – enter a 'sleeping phase'. The dermal matrix loses its structure and the skin loses its firmness, fixing in long term lines and accentuating wrinkles.

To fight this genetically programmed inversion of the triangle of beauty, Codif Recherche et Nature has developed an extract of fertile bases of *Undaria pinnatifida* called Matrigenics.14 G. This new active ingredient is rich in wakamic ester. Its activity is to reactivate genes that have gone to sleep.



Undaria pinnatifida (wakame).

Undaria pinnatifida

Undaria pinnatifida, also called wakame, is a brown macro-alga from Asia where it is grown on ropes and then eaten. It has been introduced into a large number of areas all around the world, either by ships or with Japanese oyster spat. Codif Recherche et Nature cultivates wakame in a protected area of the Rance estuary (Brittany – France) on a system of submerged ropes.

The blade of *Undaria pinnatifida* is denticulated with a central nerve running through it. The stipe is flat. At maturity, the edges of the stipe widen and become wavy (Fig. 2). These new tissues called fertile bases or mekabu contain the spores by which the species is able to reproduce.

When released into the sea, the spores swim to a rocky substrate where they attach themselves and germinate to create a new alga. The fertile bases represent a concentration of life that not only ensures the reproduction of the algae but its survival across the centuries.

To assess the benefit of these fertile bases for ageing skin, Codif Recherche et Nature isolated them from the rest of the alga to extract their compounds. Their laboratory has discovered a sulphated galactofucan called wakamic ester. This new molecule is able to activate the genes involved in the synthesis and organisation of the main components of the extra cellular matrix: collagen, elastin and proteoglycans.

Fourteen genes involved in restructuring the dermal matrix reactivated

The effect of Matrigenics.14 G (now referred to as 'the *Undaria pinnatifida* extract') on the gene's expression of the extra-cellular matrix has been evaluated on

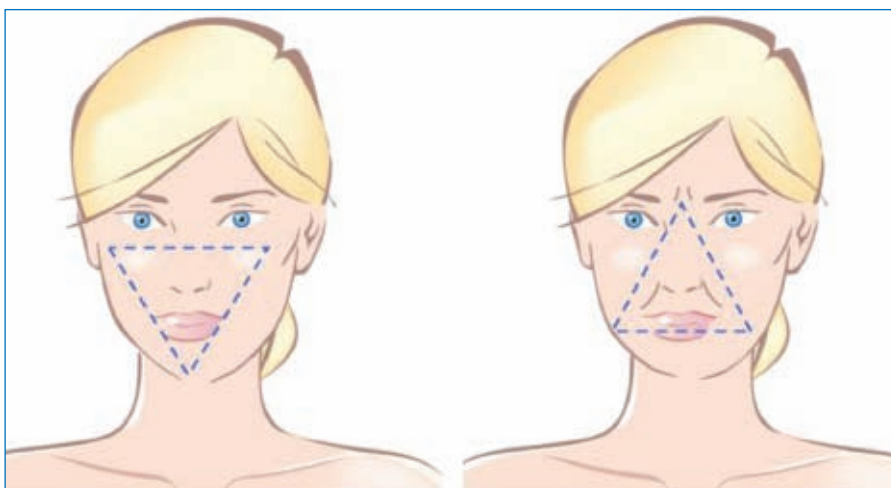


Figure 1: Inversion of 'triangle of beauty' with ageing.

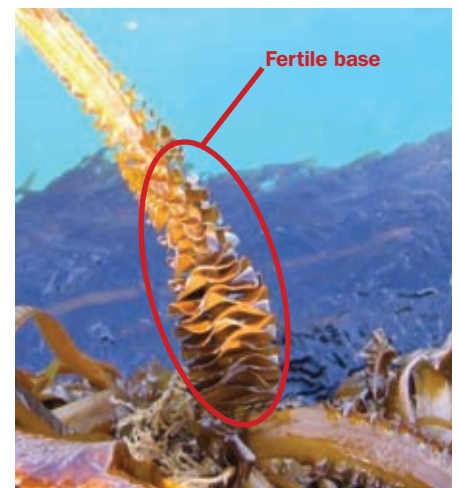


Figure 2: *Undaria pinnatifida* cultivated on ropes.

human dermal fibroblasts cultivated with 2% of active ingredient for 24 hours. The gene analysis has been carried on using DNA arrays.

The *Undaria pinnatifida* extract reactivates genes linked to collagen expression (Fig. 3).

The *Undaria pinnatifida* extract stimulates the expression of proteins involved in collagen maturation such as:

- Prolyl 4-hydroxylase P4HA1 (+61%) and P4HA2 (+30%): which both have an effect on the early stage of post-translational collagen modification.
- Lysyl oxydase LOX (+50%) and Lysyl oxydase-like 2 LOXL2 (+43%): which have an effect on a later stage of collagen synthesis.

In addition it stimulates the expression of:

- Collagen 1 (alpha chain 1) by +15% (effect illustrated in Figure 4).
- Collagen 4 (alpha chain 2) by +20%.
- Collagen 8 by +37% which is a FACIT (fibril-associated collagens with interrupted triple helices) which binds collagen fibres to their environment.
- Lumican (LUM) by +72%, which is a proteoglycan of the SLRP (small leucine-rich proteoglycan) family which binds to collagen fibres to control their organisation (the space between fibres).
- Decorin (DCN) by +23%, which is also a proteoglycan of the SLRP (small leucine-rich proteoglycan) family which binds to collagen fibres.

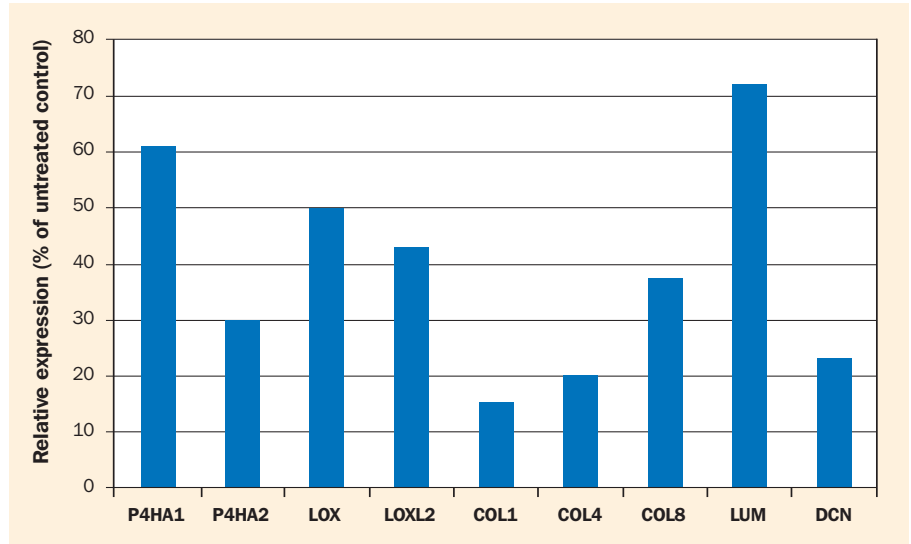


Figure 3: Effect of Matrigenic.14 G on human dermal fibroblast gene expression, linked to collagen synthesis.

The *Undaria pinnatifida* extract reactivates genes linked to elastic fibre expression (Fig. 5).

The *Undaria pinnatifida* extract stimulates the expression of several genes involved in elastin synthesis and maturation such as:

- Elastin by +21% (effect illustrated in Figure 6).
- Fibrillin 1 by +36%, which participates in elastic fibre maturation.
- Lysyl oxydase LOX by +50% and Lysyl oxydase-like 2 LOXL2 by +43%; both of these are involved in elastin maturation.
- TIMP2 by +18%, which inhibits

gelatinase A (or MMP2) activity, which breaks down elastin (elastolysis).

The *Undaria pinnatifida* extract reactivates genes linked to hyaluronic acid expression.

The *Undaria pinnatifida* extract also stimulates expression of genes involved in the synthesis and the activity of hyaluronic acid such as:

- Hyaluronan synthase HAS2 (by +68%), this is the enzyme which synthesises hyaluronic acid.
- Hyaluronate receptor CD44 (by +31%), which is a receptor for hyaluronic acid which promotes cellular migration.

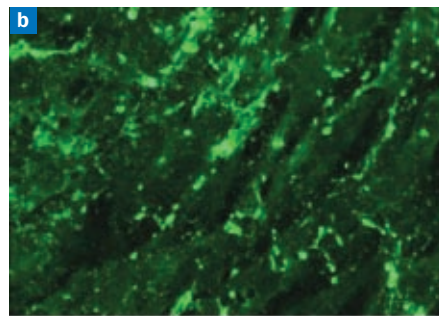
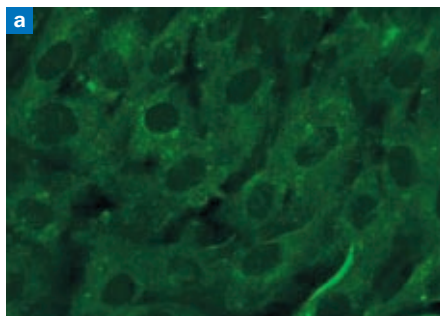


Figure 4: Immunolabelling of type 1 collagen fibres produced by human fibroblasts, a) untreated or b) treated with 2% Matrigenic.14 G.

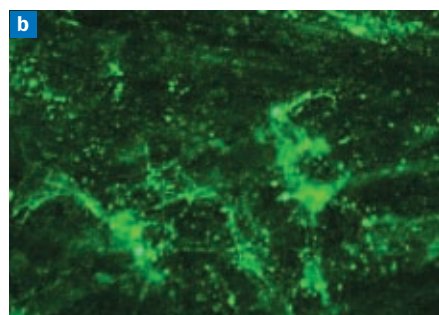
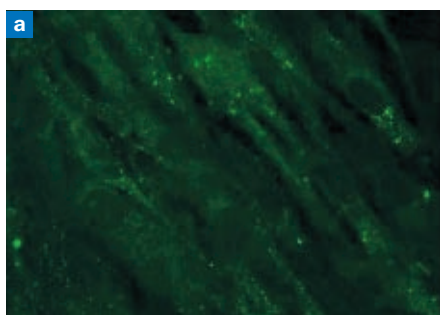


Figure 6: Immunolabelling of (tropo)elastin fibres produced by human fibroblasts, a) untreated or b) treated with 2% Matrigenic.14 G.

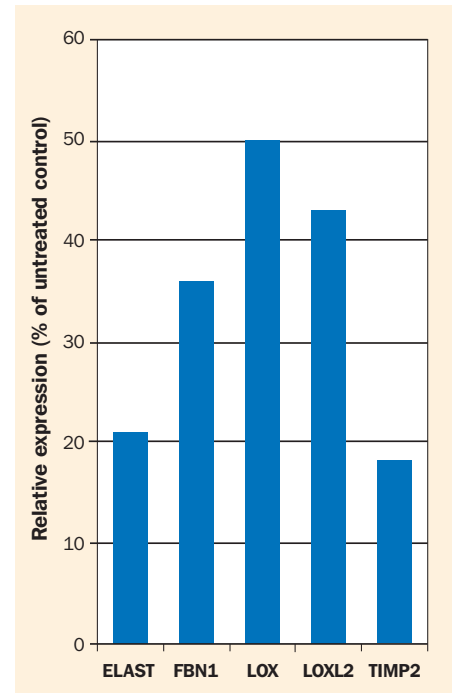


Figure 5: Effect of Matrigenic.14 G on human dermal fibroblast gene expression, linked to elastin synthesis and maturation

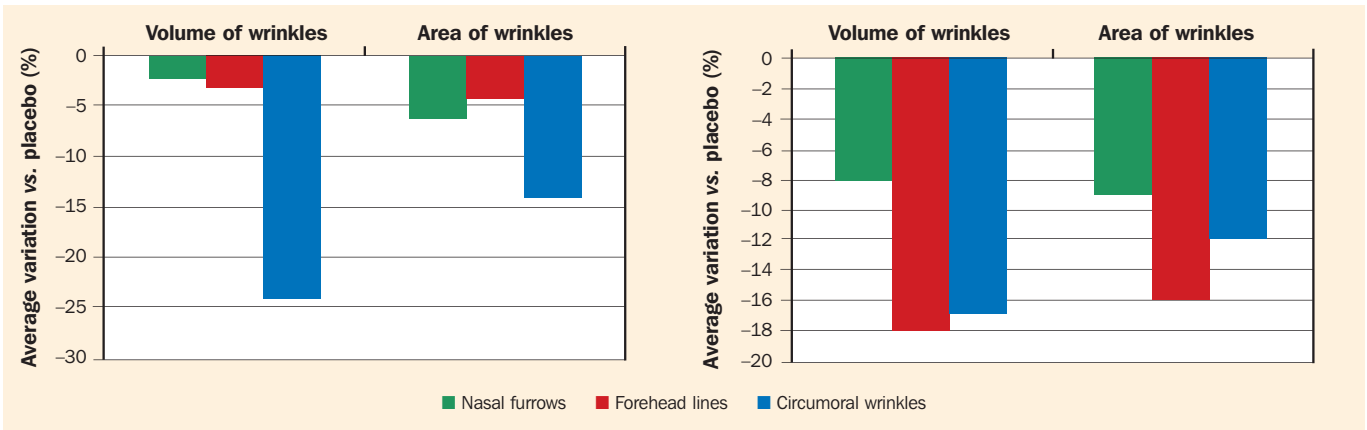


Figure 7: Effect of *Matrigenics.14 G* on the volume and area of forehead lines, circumoral wrinkles and nasal furrows a) after 14 days and b) after 28 days.

In vivo evaluation of the anti-ageing effect of the *Undaria pinnatifida* extract

The anti-ageing effect of the *Undaria pinnatifida* extract was measured using a new fringes projection technology named Face Scanner III-EO, recently developed by the company Eotech (Marcoussis, France). This technology uses the technique of fringes projection with 180° configuration. The machine can assess the signs of facial ageing in 3D.

The *Undaria pinnatifida* extract was tested at 2% in a cream against a placebo, by two panels of 22 volunteers, applying the product twice a day. The effect of the *Undaria pinnatifida* extract on forehead lines, nasal furrows and circumoral

wrinkles was evaluated after 14 and 28 days of treatment. Average results are presented in Figure 7, with data expressed versus placebo.

Effect on the forehead lines

After 14 days of application the *Undaria pinnatifida* extract significantly reduces the volume (-23.8%) and the area (-14.4%) of forehead lines (Fig. 8). It reduces them by 17% and 12% after 28 days.

Effect on the nasal furrows

The volume and area of nasal furrows are reduced by 2% and 6% respectively after 14 days and by 8% and 9% after 28 days (Fig. 9).

Effect on the circumoral wrinkles

The *Undaria pinnatifida* extract reduces the volume and area of circumoral wrinkles by 3% and 4% after 14 days and by 18% and 16% after 28 days.

Conclusion

Thanks to its richness in Wakamic ester, *Matrigenics.14 G* activates 14 genes involved in the synthesis of the main components of extra cellular matrix: collagen, elastin and hyaluronic acid. In only 14 days *Matrigenics.14 G* restructures the dermis and reduces wrinkles volume and area, thus acting against inversion of the triangle of beauty and the accentuation of negative expressions.

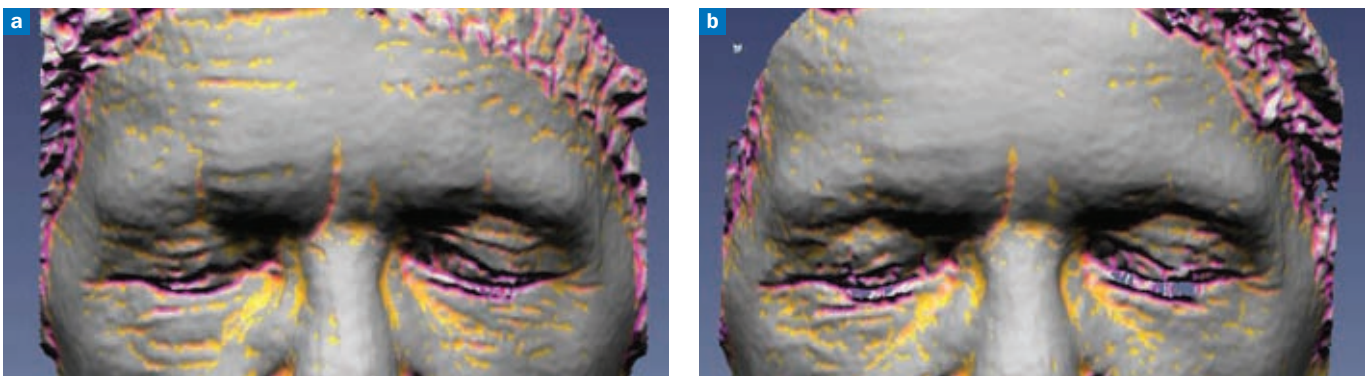


Figure 8: View of the effect of *Matrigenics.14 G* on forehead wrinkles and forehead lines of a volunteer a) before treatment and b) after 28 days.

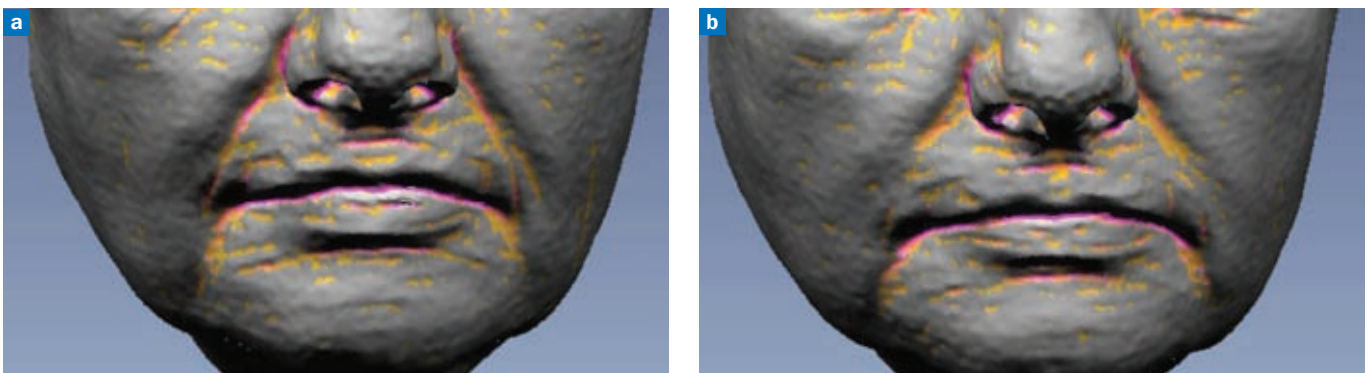


Figure 9: View of the effect of *Matrigenics.14 G* on nasal furrows and circumoral wrinkles of a volunteer a) before treatment and b) after 28 days.