NEW DATA
ON SOOTHING POTENTIAL

« THE S.M.A.R.T MULTIFUNCTIONAL REFERENCE »

S SOOTHING
M MOISTURIZING
A ANTI-AGING
R RESTRUCTURING
T TOUCH

FUCOGEL® New Data | January 2018 – V1| By SOLABIA
IN BRIEF

FUCOGEL® is an anionic polysaccharide (mean molecular weight $10^6$ Da) prepared through bacteria fermentation from non-GMO vegetable substrates. It comprises galacturonic acid, L-fucose and D-galactose.

It is distinguished by its multifunctional efficiency combining moisturizing, anti-aging, restructuring and soothing effects with sensory properties. It is the presence of fucose within its structure that gives FUCOGEL® an affinity for keratinocyte receptors and contributes to the diffusion of cellular messages. Among these, we find the stimulation of sirtuin-1, marker of cellular longevity, essential to the fight against aging. Its ability to stimulate sirtuins also results in the activation of epidermal differentiation (stimulation of loricrine and involucrine) allowing FUCOGEL® to regenerate the barrier function and optimize hydration, especially as it offers also hydrating properties, prolonged and progressive, complementary to that of another polysaccharide, hyaluronic acid.

The immediate soothing effect of FUCOGEL® is characterized by its ability to reduce the painful sensation of tingling and irritation from 5 minutes, making this active ingredient a reference for sensitive and reactive skin. Its unique mode of action has been the subject of a study on an exclusive cell model developed in collaboration with Pr. Misery (University of Brest, France), world reference in neurodermatology. Thus, FUCOGEL® inhibits the release of substance P mediated by ASICs sensitivity receptors (Acid-sensing ion channel) in response to an irritant such as lactic acid.

This study was the subject of an international publication in the Experimental Dermatology, a great renown journal and a presentation at two international dermatology congresses in 2017: the WCI (World Congress on Itch) and the 47th meeting of the European Society for Dermatological Research (ESDR).

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SCIENTIFIC BACKGROUND

Keratinocytes possess on their surface some receptors necessary for cellular communication and the activation of many physiological reactions. These receptors, called lectins, have a particular affinity for glycans such as rhamnose or fucose. Thus, the cosmetic contribution of exogenous glycans (polysaccharides for example) rich in fucose makes it possible to modulate various reactions and synthesis within the skin. This explains the ability of FUCOGEL® to stimulate, among other things, the synthesis of epidermal sirtuin-1, involucrine and loricrin for an anti-aging and restructuring effect.

The presence of fucose receptors also explains the anti-inflammatory power of fucose-rich polysaccharides, allowing inhibiting the production of pro-inflammatory molecules (cytokines, prostaglandins) by keratinocytes. But this property alone cannot explain the immediate soothing power of FUCOGEL® observed in vivo, during a stinging test after aggression with lactic acid.

The sensations of pain and tingling involved, witnessing a cutaneous neurogenic inflammation, follow the release of substance P (neuromediator) mediated by the activation of different sensitivity receptors such as TRPVs or ASICs. In order to describe the mode of action of FUCOGEL®, a unique keratinocyte / neuron cell model was developed with Pr. Misery. This model allows to predict in vitro the soothing effect of an active ingredient by inhibiting the release of substance P induced by lactic acid, under controlled pH conditions, making it possible to identify the biological pathway (TRPVs, ASICs, etc.) by which the active ingredient presents its soothing effect. This exclusive model offers a mechanistic answer that the stinging test, reference test did not give.

Thus, FUCOGEL® inhibits the release of substance P mediated by ASICs receptors. It is the first active on the market to act by this biological pathway, making this active ingredient an international reference in neurocosmetics for the soothing of the skin.
### SUMMARY OF NEW PUBLISHED RESULTS

- **Article in Experimental Dermatology:** *A new tool to test active ingredient using acid lactic in vitro, a help to understand cellular mechanism involved in stinging test: an example using a bacterial polysaccharide (Fucogel®).*


### INHIBITION OF NEUROGENIC INFLAMMATION VIA ASICs SIGNALING

*Exclusive in vitro study on keratinocytes/neurons co-culture treated in the medium with FUCOGE® at 0.1% in water and lactic acid at 0.1%. Quantification of the Substance P released by ELISA kit.*

- Lactic acid induces the release of substance P by keratinocytes and neurons.

- **The release of substance P by lactic acid is under an acidic mechanism.**
  In fact, when the lactic acid is neutralized there is no release of substance P.

![Substance P release](chart.png)

- **Without lactic acid**
- **With lactic acid**
- **With neutralized lactic acid**

<table>
<thead>
<tr>
<th></th>
<th>Keratinocytes</th>
<th>Neurons</th>
</tr>
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<tbody>
<tr>
<td>Without lactic acid</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>With lactic acid</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>With neutralized lactic acid</td>
<td>1</td>
<td>1</td>
</tr>
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*p<0.05*
Lactic acid acts by an acidic mechanism, inducing an entry of calcium that activates the cell receptors of sensitivity like TRPVs (Transient Receptor Potential Vanilloide) and ASICs (Acid-sensing ion channel) and thus the release of Substance P by cells.

**ILLUSTRATION OF THE MECHANISM OF ACTION**

When receptors TRPVI and ASICs are subjected to lactic acid, they become activated and change conformation, resulting in opening of the cation channel and the massive influx of calcium ions into cells (calcium flash). This calcium influx marks the beginning of the cellular response resulting in the end by the release of inflammation mediators such as the substance P.

**CONCLUSION :**

The neutralization of lactic acid doesn’t induce a calcium entry.
**Conclusion**:

FUCOGEL® inhibits the release of substance P induced by the activation of the ASICS pathway by lactic acid. Thus, FUCOGEL® decreases the neurogenic inflammation and has great anti-inflammatory and soothing properties.

The results obtained in this new exclusive study could be correlated with the soothing effect of FUCOGEL® observed *in vivo*.

**Comments**:

- Considering that FUCOGEL® doesn’t induce a significant modification of the pH, it is not able to act on the substance P release through any lactic neutralization.
- Bibliographic data show that the range of pH for the activation of TRPV1 and for the entrance of calcium into the cells is not compatible with the culture conditions applied in the defined protocol[1]. Then the FUCOGEL®’s biological pathway couldn’t be related to the TRPV1 receptor activation. On the contrary, the activation of ASICS is fully complying with the chosen experimental conditions[2].

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**SOOTHING ACTIVITY**

*In vivo study* on volunteers with sensitive and reactive skin. One application of FUCOGEL® at 3% vs. Placebo on the nasolabial fold after lactic acid aggression. Soothing effect evaluation after 5 minutes (stinging test).

**Conclusion**:

Only 5 minutes after application, FUCOGEL® has a soothing effect on irritated and hypersensitive skins by decreasing the tingling sensation. FUCOGEL® relieves quickly from aggressions and restore the well-being and comfort of the skin.