A revolution in the treatment of dark spots.
THE solution for treating "dark spots pollution-induced".
Codif Laboratories have discovered a revolutionary molecule which is able to interact with the pigmentary synapses to treat dark spots pollution-induced.

A molecule with unique folding.

A molecule that was discovered as part of a national collaborative research programme: POLYMER.

A molecule that is effective against dark spots within 2 weeks use.

A molecule found to be effective by 96% of users on reducing the number of pigmentary spots.
REDUCES MELANIN SYNTHESIS POLLUTION INDUCED

It had already been shown that pollution induces inflammation, itself involved in melanogenesis activation. But a recent study definitively confirmed that pollution is directly involved in increasing the number of pigmented spots on the cheeks\(^{(1)}\). To treat dark spots pollution-induced, EPS WHITE reduces inflammation pollution induced.

EFFICACY ON DARK SPOTS POLLUTION INDUCED + PIGMENTARY SYNAPSE INNOVATION

INHIBITS THE FORMATION OF PIGMENTARY SYNAPSES TO REDUCE MELANIN TRANSFER

Transfer of melanin from melanocytes to keratinocytes is physically possible due to mutual recognition between the two cells. This recognition occurs by a keratinocyte receptor fixing onto a melanocyte receptor. This conjuncture is called a pigmentary synapse\(^{(2)}\).

EPS WHITE is able to fix the melanocyte receptor so that it cannot communicate with the keratinocyte and so prevents formation of the pigmentary synapse.

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A CLEAR LINK

Pollution - Inflammation - Dark spots

Our laboratories have shown that pollution induces an increase in the pro-inflammatory enzyme COX2 in the epidermis. However COX2 activates prostaglandins, known for stimulating melanogenesis.

Pigmentary synapse and melanin transfer

EPS WHITE reduces formation of pigmentary synapses by 35%.
A COMPOSITION AND SPECIFIC CONFIGURATION FOR INTERACTING WITH PIGMENTARY SYNAPSES.

The formation of pigmentary synapses involves osidic receptors, i.e. the recognition of sugar residues. EPS WHITE is a sugar polymer with an unparalleled structure which enables it to reach the site and interact with the formation of pigmentary synapses.

A SCIENTIFIC DISCOVERY

EPS WHITE is a molecule that came out of the POLYMER collaborative research programme involving a university laboratory, three private companies and a technology transfer centre. Financed by the Government, the project brought together the top experts in cutaneous biology and marine biotechnology. The project was to discover new molecules and to develop new study models.

This is the first marine Exopolysaccharide in which two amino acids have been identified: serine and alanine. These two hydrophobic amino acids induce folding of the molecule in the form of microvesicles and so facilitate its penetration into the skin to interact with the pigmentary synapses. The discovery of this molecule was published in the literature\(^3\).

\(^3\) Structure of an Amino Acid-Decorated Exopolysaccharide Secreted by a Vibrio alginolyticus Strain. S. Drouillard (and al). Mar. Drugs 2015, 13, 6723-6739
Configuration of an EPS not containing hydrophobic amino acids.

Folding induced by the two amino acids contained in EPS WHITE and microscopic observation of the microvesicle structure.

100nm
**IN-VITRO**

- 35% inhibition in the formation of pigmented synapses.
- 45%** protection against production of COX2 pollution induced.
- 71%* protection against melanin synthesis pollution induced.
- 39% protection against production of COX2 UVs induced.
- 81% protection against synthesis of melanin UVs induced.

**IN-VIVO**

After 2 weeks treatment:
- 6% average reduction in dark spots and up to 38% reduction.

After 4 weeks treatment:
- 13%* average reduction in dark spots and up to 57% reduction.

After 8 weeks treatment:
- 20%* average reduction in dark spots and up to 60% reduction.
- 12%** average reduction in dark spots area and up to 51% reduction.
- 96% of users observed a reduction in dark spots.
- 92% of users found their pigmentation to be more uniform.
- 92% of users found their skin tone transformed after each application.

*p<0.05 - **p<0.01 Student test
Visualization of melanin synthesis (in blue) in explants exposed to car exhausts 1H/day for 9 days

Twice daily application on the face of a formulation containing 1% EPS WHITE. Change in number of dark spots during treatment.

Without EPS WHITE

With 1% EPS WHITE
## INDICATIVE FORMULATION

**Intensive Dark Spots Corrector**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Chemical Name / Trade Name</th>
<th>INCI Name</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>EMULFREE CBG (1)</td>
<td>Isostearyl Alcohol &amp; Butylene Glycol Cocoate &amp; Ethylcellulose</td>
<td>4.00</td>
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<tr>
<td>A</td>
<td>CRODAMOL GTCC / MIGYOL 812 / WAGLINOL (2)</td>
<td>Caprylic/Capric Triglyceride</td>
<td>3.00</td>
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<tr>
<td>A</td>
<td>DPPG CG (1)</td>
<td>Propylene Glycol Dipelargonate</td>
<td>3.00</td>
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<tr>
<td>A</td>
<td>LEXFEEL D5 (3)</td>
<td>Neopentyl Glycol Diheptanoate &amp; Isododecane</td>
<td>4.00</td>
</tr>
<tr>
<td>A</td>
<td>PHENOXYETHANOL (4)</td>
<td>Phenoxyethanol</td>
<td>0.80</td>
</tr>
<tr>
<td>B</td>
<td>DEMINERALIZED WATER</td>
<td>Aqua</td>
<td>74.98</td>
</tr>
<tr>
<td>C</td>
<td>CARBOPOL ETD 2020 (1)</td>
<td>Acrylates/C10-30 Alkyl Acrylate Crosspolymer</td>
<td>0.30</td>
</tr>
<tr>
<td>D</td>
<td>ELESTAB CPN (2)</td>
<td>Chlorophenesin</td>
<td>0.27</td>
</tr>
<tr>
<td>E</td>
<td>BIDISTILLED GLYCERIN CODEX (5)</td>
<td>Glycerin</td>
<td>7.40</td>
</tr>
<tr>
<td>E</td>
<td>XANTHAN GUM (6)</td>
<td>Xanthan Gum</td>
<td>0.20</td>
</tr>
<tr>
<td>F</td>
<td>SODA (SOLUTION 5 N) (7)</td>
<td>Aqua &amp; Sodium Hydroxide</td>
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</tr>
<tr>
<td>G</td>
<td>SYMDIOL 68 (8)</td>
<td>1,2-Hexanediol &amp; Caprylyl Glycol</td>
<td>0.50</td>
</tr>
<tr>
<td>G</td>
<td>FRAGRANCE</td>
<td>Fragrance</td>
<td>0.10</td>
</tr>
<tr>
<td>G</td>
<td>EPS WHITE P (9)</td>
<td>Glycerin &amp; Aqua &amp; Phenoxyethanol &amp; Saccharide Isomerate</td>
<td>1.00</td>
</tr>
</tbody>
</table>

(1) GATTEFOSSE FRANCE SA, (2) AMI, (3) SACI-CFPA, (4) BIOPHILL, (5) QUIMASSO FRANCE EURL, (6) UNIVAR (LAMBERT RIVIERE), (7) BRENNTAG, (8) SAFIC-ALCAN (SOCHIBO), (9) CODIF Recherche et Nature

**PROCEDURE**

- Mix phase A, ambiante temperature.
- Heat B to 75 °C.
- Add C under emulsifier 1500 rpm for 15 minutes.
- Add D under emulsifier 1500 rpm for 5 minutes.
- Cool down to 35 °C under pale.
- Add the premix E under emulsifier 1500 rpm for 10 minutes.
- Add F under emulsifier 1500 rpm for 10 minutes.
- Perform the bi-gel gradually adding the fatty phase A in the aqueous phase (4 steps) under emulsifier 1500 rpm. Between each addition, stir 5 minutes to let the fat phase incorporates well with the aqueous phase: the resulting mixture becomes white and shiny.
- Mix under 2500 rpm for 15 minutes.
- Add one by one ingredients of phase G under pale and let stir for 10 minutes.
Water soluble ingredient to be used at 1% in:

- An anti-pollution protection formula along with **PHYCOSACCHARIDE AP**
- An anti-pollution eye contour with **CITYGUARD+**
- A daily anti-stress range combined with **AREAUMAT PERPETUA**

**EPS WHITE P**
- water (and) glycerin (and) phenoxyethanol (and) saccharide isomerate

**EPS WHITE PA**
- water (and) glycerin (and) phenetyl alcohol (and) saccharide isomerate