A CUTTING-EDGE MOLECULE FOR A RADIANT SKIN TONE
THE CULTURE OF A BRIGHTER SKIN (I)

Skin brighteners use and consumers’ demand is growing worldwide.

- In **Western countries**, skin brighteners are applied for the prevention and treatment of irregular hyperpigmentation, resulting in an evener skin tone.

- In **Asia**, brighter skin is a symbol of beauty and femeninity. The use of skin brightening agents is widely extended by traditional beliefs.
  - The need of whitening the skin is so high that most of anti-aging products contain also whitening ingredients and UV filters.
THE CULTURE OF A BRIGHTER SKIN (II)

Japan
Sales of Whitening products are 15-17% of Skin Care sales

China
30% of people use Skin Whitening products

Thailand
Even more population (60%) uses Skin Whitening products
THE CULTURE OF A BRIGHTER SKIN (III)

Whitening and brightening products account for 60% of new products among the top ethical beauty launches (Mintel GNPD Beauty Innovation)

Even skin tone

Anti-age spots
GROWTH IN SKIN LIGHTENING BY MARKET

(US $ Million)

<table>
<thead>
<tr>
<th>Country</th>
<th>Growth Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>21%</td>
</tr>
<tr>
<td>Thailand</td>
<td>20%</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>6%</td>
</tr>
<tr>
<td>United Arab Emirates</td>
<td>37%</td>
</tr>
<tr>
<td>Morocco</td>
<td>19%</td>
</tr>
<tr>
<td>Egypt</td>
<td>12%</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>1,000+%</td>
</tr>
<tr>
<td>United States</td>
<td>-11%</td>
</tr>
<tr>
<td>Greece</td>
<td>31%</td>
</tr>
<tr>
<td>Slovakia</td>
<td>n/a</td>
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</tbody>
</table>

AC Nielsen, 2007
The colour of the skin and hair depends on the amount, distribution and type of melanin.

- Melanins are pigmented biopolymers synthesised in melanocytes in the DEJ (Dermo-Epidermal Junction).
- Melanosomes with melanins migrate and they are transferred to keratinocytes in skin.
• Typical pigmented changes appear during intrinsic aging and photoaging:

**HYPERPIGMENTATION**
melasma, freckles, age spots and senile lentigines

- abnormal accumulation of melanin
- acute or persistent UV exposure
Inhibition of melanin synthesis by inhibition of tyrosinase activity.

Tyrosinase: key enzyme of melanogenesis.

Need for novel skin brightening agents with increased **efficacy** and improved **safety** profiles.
According to Dooley\(^1\), new depigmentation products should include the following desirable features:

<table>
<thead>
<tr>
<th>PROPERTIES</th>
<th>chromabright®</th>
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<tbody>
<tr>
<td>Inhibition of mammalian tyrosinase</td>
<td>✓ (human tyrosinase)</td>
</tr>
<tr>
<td>Lack of toxicologic or mutagenic potential</td>
<td>✓ (impeccable safety profile)</td>
</tr>
<tr>
<td>Clinical efficacy</td>
<td>✓ (proven \textit{in vivo})</td>
</tr>
<tr>
<td>Formulation stability</td>
<td>✓ (high stability)</td>
</tr>
<tr>
<td>Novelty and patent protection</td>
<td>✓</td>
</tr>
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</table>

**PHOTOPROTECTIVE EFFECT**

prevention of UV-induced skin damage

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**CHROMABRIGHT® STABILITY**

Tested in an O/W emulsion

<table>
<thead>
<tr>
<th>INGREDIENT</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>qsp 100</td>
</tr>
<tr>
<td>Mineral Oil (Paraffinum Liquidum)</td>
<td>10</td>
</tr>
<tr>
<td>Polymethylacrylamide, C13-14 Isoparaffin, Laureth-7</td>
<td>3</td>
</tr>
<tr>
<td>CHROMABRIGHT®</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Chromabright® proved to remain stable after 6 months and at different pH final formulations.
Completely safe profile:

- Ocular irritation (HET-CAM test).
- Phototoxicity.
- Cytotoxicity on human epidermal keratinocytes.
- Cytotoxicity on 3T3 fibroblasts.
- Bacterial reverse mutation test (Ames test).
- Cytotoxicity on human primary melanocytes.
- Skin sensitisation.

Chromabright® showed no signs of toxicity in any of the tests above.
CHROMABRIGHT® EFFICACY

**IN VITRO**

- Inhibition of mushroom tyrosinase activity.
  - It is the most used assay to assess potential depigmenting agents.
- Inhibition of endogenous human tyrosinase activity.
  - This assay should be considered much better than mushroom tyrosinase.
- Depigmenting effect on human melanocytes.
- Melanogenesis inhibition on human epidermal melanocytes.
- Photoprotective effect on human epidermal keratinocytes.

**IN VIVO**

- Skin brightening effect on human volunteers.
IN VITRO EFFICACY (I)

1. Tyrosinase inhibition

Mushroom tyrosinase

- L-Dopa (tyrosinase substrate) was digested in the presence of 1mM Chromabright® and the enzyme.
- Absorbance variations were measured at 475 nm.
- Kojic acid 0.1mM was used as positive control.

37% inhibition of mushroom tyrosinase activity

Endogenous human tyrosinase

43% inhibition of endogenous human tyrosinase activity
2. Depigmenting effect on human melanocytes cultures

- Incubation of plated human melanocytes for 5 days.
- Daily addition of fresh medium containing 0.1mM Chromabright® or Kojic Acid.
- Kojic acid 0.1mM was used as positive control.
- The lightening efficacy was assigned by counting the cells showing melanin staining and the total number of cells.

Chromabright® exhibits a better depigmenting effect than Kojic Acid on human melanocytes.
3. Melanogenesis inhibition on human melanocytes cultures (I)

- Primary human melanocytes (HEMn-DP) cells were seeded and allowed to grow for 2 weeks.
- Melanocytes were treated on days 1, 3, 6, 8, 10, 13, 15 and 17 with:
  - Chromabright® (5µM, 10µM, 100µM, 150µM and 200µM)
  - Hydroquinone (10µM)
  - MAP (Magnesium Ascorbyl Phosphate) (10µM)
  - Kojic Acid (10µM)
  - Arbutin (10µM)
- Control: medium without treatment.
- After 20 days of culture, melanin concentration was determined by measurement of absorbance at 450nm and values were normalised respect to the number of cells per well.

Chromabright® inhibited melanogenesis at all tested concentrations, in a dose-dependent manner.
3. Melanogenesis inhibition on human melanocytes cultures (II)

By optical microscopy

Control  

chromabright® 200µM  

chromabright® 10µM  

Hydroquinone 10µM

Similar activity at the same concentration, but Chromabright® did not present cytotoxicity while Hydroquinone cytotoxic effect was clearly observed, at the dosages tested.

Chromabright® melanogenesis inhibition efficacy was higher than Arbutin, Kojic Acid and MAP at the same concentration (10µM).
4. Cellular photoprotection

NRU photoprotection test in Human Epidermal Keratinocytes

- Test based on the determination of the protective effect of a chemical when tested in the presence of a cytotoxic dose of simulated solar light.
- Irradiation to cells implies a decreased uptake of the vital dye Neutral Red (NR).

190% increase in cell viability

Chromabright® helps to prevent the skin-damaging effects of UV radiation.
1. Brightening effect

- 20 Asian female volunteers, aged 18 to 46.
- A cream containing 0.1% Chromabright® was applied on one side of the face twice daily and a placebo cream on the other side for 60 days.

- Measurements were taken before application, after 30 and 60 days of treatment.
- Parameters used to evaluate the effects:
  - L* (Luminance): represents the relative brightness from total darkness (L*=0) to absolute white (L*=100)
  - ITA° (Individual Typological Angle): categorises skin colour, obtained combining L* and b* (yellow-blue colour axis)

A cream containing 0.1% Chromabright® induced a significant brightening effect after 30 and 60 days.
2. Depigmenting effect

- 10 volunteers, aged 18 to 70, with melasma and/or actinic lentigines applied a cream containing 0.5% Chromabright® on their face and/or hands twice a day for 60 days.

- Clinical and iconographic controls were performed at the beginning of the study, and after 30 and 60 days of application.

80% of the volunteers with melasma and 77.8% with lentigines experienced a significant improvement after 60 days.
COSMETIC BENEFITS

**chromabright®**

- **Safety & efficacy together**

  - Pure molecule
    - High stability and keeps purity of 100%
  - High efficacy in short time
    - Significant brightening effect in only 2 months
    - High depigmenting power after 30 days
  - Photoaging prevention
    - Cellular photoprotection demonstrated
  - Safety
    - Completely safe toxicological profile
DESCRIPTION
A new patented ingredient designed for skin brightening applications that shows neither cytotoxic effects, nor any irritation or sensitisation reaction.

APPEARANCE
Powder.

INCI
Dimethylmethoxy Chromanyl Palmitate.

PROPERTIES
It induces a significant lightening effect on the skin, at the same time that fights against photoaging.

APPLICATIONS
Chromabright® can be incorporated in cosmetic formulations containing oil or silicon phases where a brightening effect on the skin is desired.

DOSAGE
0.1-0.5%
A CUTTING-EDGE MOLECULE FOR A RADIANT SKIN TONE

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