DERMA-LUCIA R & D FOR ANTI-AGING

Derma-Lucia Skinceuticals LLC
BIO-FD&C Co., Ltd

Marketing Office: located in Austin, TX USA (512) 751-3922 ☎
Main Office located in Incheon of S. Korea 82-32-811-2027☎
Research Center located in Jeonnam of S. Korea 82-61-373-8381☎

www.biofdnc.com
R&D (Advantages, Technologies)

We have established research oriented facility from a state-of-art biochemical laboratory to a manufacturing facility. And also we can produce therapeutical proteins in the scale of 300L in fermenter system of JBRC as GMP grade.

Our technologies

1. Recombinant Protein Expression and Refolding Technology
   - Genetic recombinant technology for high level protein expression. Recombinant proteins are highly valuable biological resources, such as cytokines and growth factors.

2. Functional Peptide Synthesis Technology
   - Solid phase synthesis technology using Fmoc (Boc)-chemistry
   - Technology of isolation and identification of physiologically active phytochemical-fused peptides

3. Plant Tissue Culture Technology
   - Callus induction and culture technology from various plants.
   - Genetic recombinant technology using of Ti plasmid in Agrobacterium tumefaciens.

4. Optimized Screening Technology for Atopic dermatitis from Herbal sources.
   - High throughput biochemical screening technology.

5. Stem Cell Research with Cutting-edge Technology.
   - Technology of isolation, culture, and plantation of stem cells from various human tissues.
Research Items

- **Peptide**
  - Anti-aging
  - Anti-hair loss
  - Anti-microbial activity

- **Callus**
  - Anti-oxidation
  - Anti-inflammation
  - Atopic dermatitis

- **Protein**
  - Wound healing
  - Immune function
  - Therapeutics

- **Stem Cell**
  - Regeneration
  - Transplantation
  - Stem cell therapy

---

**Innovative R&D based Business Portfolio**

- **Stem cell therapy**
  - 2010-2024

- **Pharmaceutical neuropeptides for wound healing or Alzheimer**
  - 2009-2017

- **Phytochemical fused peptides for anti-aging**
  - 2008-2016

- **Plant callus as cosmetic active ingredient for anti-aging**
  - 2006-2014

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New Drugs
Technologies

Functional Peptide
- Anti-aging
- Anti-hair loss
- Anti-microbial activity

Plant Stem Cell
- Anti-oxidation
- Anti-inflammation
- Anti-atopic dermatitis

Recombinant Protein
- Wound healing
- Immune function
- Therapeutics

Stem Cell Research
- Regeneration
- Transplantation
- Stem cell therapy

Solid Phase Peptide Synthesis Tech
Structure based on Recombinant Tech
DDS Application
Biosensor Application

Genetic Recombinant Tech

Stem Cell Manipulation Tech
- Apical meristem cell isolation
- Root meristem cell isolation
- Callus induction
- Elicitor treatment in callus culture process
- Unique wavelength treatment in callus culture process
- Ultrasonic application to plant cells
- Radiofrequency application to plant cells
- Genetic recombinant technology using of Ti plasmid

Photoperiod or Elicitor treatment
Light Emitting Diodes
Ultrasonic Wave

05
Peptides are short amino acid sequences that are components of larger proteins, such as collagen. Peptides are much more stable than protein.

Solid-phase synthesis is the most common technique for peptide synthesis. Usually, peptides are synthesized from the carbonyl group side (C-terminus) to amino group side (N-terminus) of the amino acid chain in this method, although peptides are synthesised in the opposite direction in cells.

**Peptide = chain of amino acids**
Manufacturing Method of Peptide

Procedure of Peptide Synthesis

1. Resin(solid) Swelling
2. Amino acid activation
3. Amino acid conjugation as peptide sequence
4. Completion of Amino acid binding
5. Cleavage from peptide-conjugated resin
6. Concentration/Crystallization

Purification & Lyophilization

1. Purification by Prep, HPLC
2. Freeze dry(Powder)

BIO-Assay and Ingredient for cosmetic
## Neuropeptides

<table>
<thead>
<tr>
<th>Trade name</th>
<th>INCI Name</th>
<th>Applications</th>
<th>Anti-aging</th>
<th>Wound healing</th>
<th>Whitening</th>
<th>Anti-oxidation</th>
<th>Anti-inflammation</th>
<th>Hair-Care</th>
<th>Others</th>
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**Images:**
- Enkephalin
- Neoendorphin
- alpha-Endorphin
- beta-Endorphin
- gamma-Endorphin
- DP-Enkephalin
- DP-Neoendorphin
- Neuropeptide-1
- Neuropeptide-2
- Neuropeptide-3
- Niacin-Enkephalin

**Derma Lucia**

08
# Cosmetic Peptides

<table>
<thead>
<tr>
<th>Trade name</th>
<th>INCI Name</th>
<th>Applications</th>
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<td>Phytopeptide-1</td>
<td>Caffeoyl Tripeptide-1</td>
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<td>Gallovax™</td>
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<td>Redovax</td>
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<tr>
<td>Symvastin</td>
<td>Digalloyl Tetrapeptide-19</td>
<td>VV</td>
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**Chemical Structures:**

- **Gold Binding Peptide-1**
- **Phytopeptide-1**
- **Caffeoyl Neuropeptide-1 (NP7)**
- **Gallovax™**
- **Redovax**
- **Symvastin**
January 3, 2008

Sanghyun Moh
Bio-FD&C Co., Ltd.
24BL-8LT, Namdong Ind. Complex, 451-7
Nonhyun-Dong, Namdong-Gu
Incheon 405-840
Republic of South Korea

Dear Sanghyun Moh:

PCPC File No. 18080

In response to your Form TN submission(s) for the assignment of the International Nomenclature Cosmetic Ingredient (INCI) name(s) to your material(s), please be advised that the International Nomenclature Committee has completed its review of your request.

The name(s) assigned to your material(s) is listed on the attached printout. Please check the printout for accuracy, and advise if revisions are needed.

Your name assignment(s) will be published in future editions of the International Cosmetic Ingredient Dictionary and Handbook and the International Buyer's Guide.

Petitions requesting the revision of an INCI name assignment must be filed on Form TN and accompanied by a cover letter which explains the reasoning for the change. Relevant information on chemical composition or other criteria which support the revision should also be included with the petition.

In addition, be advised that nomenclature assignments are subject to change if deemed necessary for technical accuracy or other reasons as determined by the International Nomenclature Committee.

We trust this information is helpful.

Sincerely,

Tara E. Gottschalk
Manager - Cosmetic Ingredient Database

Enclosure

PCPC FILE NUMBER: 17882

TRADE NAMES WITH ASSIGNED INCI NAMES

TRADENAME: Phytopeptide-1
Assigned INCI Name(s): MonoID: 22750 Caffeoyl Tripeptide-1
Phytopeptide-1

Structures for Phytopeptide-1

Chemical Formula: C_{23}H_{30}N_{6}O_{7}
Exact Mass: 502.22
Molecular Weight: 502.52
m/z: 502.22 (100.0%), 503.22 (25.5%), 504.22 (5.0%), 503.21 (2.2%)
Elemental Analysis: C, 54.97; H, 6.02; N, 16.72; O, 22.29

<3D Structure of Phytopeptide-1>
**Phytopeptide-1**

**Caffeic acid Derived Peptides**

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>INCI Name</th>
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<tr>
<td>Phytopeptide-1</td>
<td>Caffeoyl Tripeptide-1</td>
</tr>
<tr>
<td>NP7</td>
<td>Caffeoyl sh-Octapeptide-4</td>
</tr>
</tbody>
</table>

Phytopeptide-1 and NP7 are fused peptides in conjunction with caffeic acids

**Chlorogenic acids**

Chlorogenic acids are actually a family of esters formed between quinic acid and phenolic compounds known as cinnamic acids. The most abundant chlorogenic acid in coffee is 5-O-caffeoylquinic acid, an ester formed between quinic acid and caffeic acid.

**Caffeic acid as a strong anti-oxidant**

**Major Chlorogenic acids in Coffees**

- 3-O-Caffeoylquinic acid
- 4-O-Caffeoylquinic acid
- 5-O-Caffeoylquinic acid
- 3-O-Feruloylquinic acid
- 4-O-Feruloylquinic acid
- 5-O-Feruloylquinic acid
- 3,4-O-Dicaffeoylquinic acid
- 3,5-O-Dicaffeoylquinic acid
- 4,5-O-Dicaffeoylquinic acid
Caffeic acid Derived Peptides

- Anti-oxidation effect (Fig 1)
- Inhibition of COX-2 expression (Fig 2)
- Inhibition of Scratching (Fig 3)


Phytopeptide-1

Caffeic acid Derived Peptides

**Caffeoyl-Tripeptide-1**

- Strong anti-oxidation effect
- Enhanced Stability
- Increased Solubility

**Phytochemical-Caffeic acid**

Caffeic acid as phytochemical

- Strong anti-oxidation effect
- Anti-inflammation effect
- Low stability in the water
- Low solubility in the water

**Peptide-GHK Tripeptide**

Tripeptide as peptide

- Skin compatibility
- No anti-oxidation effect

Solid-Phase Peptide Synthesis (With Cutting-Edge Technology)
Phytopeptide-1

Radical Scavenging Effect of Phytopeptide-1

Anti-Oxidant Capacity by Reducing Free-Radicals of DPPH

Anti-Oxidant Capacity by Reducing Free-Radicals of DPPH

Phytopeptide-1(INCI Name: Caffeoyl-Tripeptide-1)
Phytopeptide-1

Stability of Phytopeptide-1

The caffeic acid can be easily oxidized in solution. But the Phytopeptide-1 (Caffeoyl-GHK) has high stability in liquid state. It didn’t change color in solution. It has strong anti-oxidation effect. It has been shown to reduce pimples or small blemishes on the skin.

After 30 days at RT
Clinical Data of Phytopeptide-1

Clinical Trials

Before

100ppm solution of Phytopeptide-1 was treated to the face for three times

After
Phytopeptide-1

Biological Mechanism of Phytopeptide-1

Genetic → Environmental → ROS → NF-kB Activation → Gene Transcription

Cytokines, Chemotactic Factors → Inflammation

ROS → Cell Death

Anti-oxidation

Phytopeptide-1 → Anti-inflammatory

Amplification

Developmental → Hormonal → ROS → Inflammation
### Product Information

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Phytopeptide-1</th>
<th>Manufacturer</th>
<th>BIO-FD&amp;C Co., Ltd (<a href="http://www.biofdnc.com">www.biofdnc.com</a>)</th>
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<tbody>
<tr>
<td>Contact</td>
<td>Sang Hyun Moh</td>
<td></td>
<td><a href="mailto:shmoh@biofdnc.com">shmoh@biofdnc.com</a></td>
</tr>
<tr>
<td></td>
<td>☎ 82-32-811-2027 Fax</td>
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<td>82-32-822-2027</td>
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</table>

| PCPC Name           | Caffeoyl Tripeptide-1    |              |                                     |
| Packing Unit        | 500ppm solution type, 10Kg/packing unit |
| Recommended Dosage in Cosmetic Formula | 1~3% |

| Characteristics     |                                                                                     |
|                     | ❖ Synthetic Peptide Materials (Caffeic acid coming from coffee tree in conjunction with GHK tripeptide) |
|                     | ❖ Solubility : 1.7g / 100 ml (H₂O)                                                 |
|                     | ❖ High Stability in Solution                                                        |
|                     | ❖ M.W. 502.5 Da                                                                    |

| Function            |                                                                                     |
|                     | ❖ Anti-Oxidation Effect                                                             |
|                     | ❖ Trouble Care Effect (Reduced Pimples on the Skin)                                 |

| IP                  |                                                                                     |
|                     | ❖ Patent Title                                                                      |
|                     | Novel Cinnamoyl Peptide Derivative Having 4-Hydroxy Substituent, Method For Preparing The Same And Cosmetic Composition Comprising The Same. |
|                     | ❖ Registered Number                                                                 |
|                     | 10-2008-0084159                                                                     |
|                     | ❖ Country / Registered Date                                                         |
|                     | KR / 2008.08.27                                                                     |

| References          |                                                                                     |
The INCI name of the Caffeoyl Octapeptide-4 is changed to the Caffeoyl sh-Octapeptide-4 by PCPC.
Chemical Formula: $C_{51}H_{89}N_{11}O_{13}$
Exact Mass: 1039.48
Molecular Weight: 1040.13
m/z: 1039.48 (100.0%), 1040.48 (56.4%), 1041.48 (20.2%), 1040.47 (4.1%), 1042.49 (2.8%), 1042.48 (2.2%)
Elemental Analysis: C, 58.89; H, 6.30; N, 14.81; O, 20.00
NP7 (CA-NP-1)

Synthesis of NP7

![Chemical Structure of NP7]

HOBt / DCC Activation

[Caffeoyl-Neuropeptide-1]

Caffeoyl-Neuropeptide-1 (ICN Name: Caffeoyl-Octapeptide-4)
Stability of NP7 High Stability of NP-7 in the Solution

Stability Test of CA-NP-1 in the Solution State at Room Temperature

[After 1 day at RT] [After 1 month at RT] [After 2 months at RT]
NP7(Caffeoyl-NP-1)

Anti-Oxidation Effect of NP7

NP7 has a highly anti-oxidation effect such as caffeic acid and Vitamin C
NP7 (Caffeoyl-NP-1)

**Anti-Inflammation Effect of NP7**

- **Type-II Collagen**
- **COX-2**
- **GAPDH**
### Clinical Data of NP7

#### Clinical Test of NP7 to 20 Patients of Atopic Dermatitis

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**Ave**: 14.70  
**S.D.**: 8.40

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**NP7** (Caffeoyl-NP-1)

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인체적용시험보고서

주바이오에프디엔씨

Cream 및 CA-NP-1의 2주간 피부 혈행
개선평가 인체적용시험 연구

2008년 7월 18일

주식회사 엘리드 피부과학연구소
Clinical Data of NP7

Improvement of Blood Circulation on Atopic dermatitis by Laser Doppler Perfusion Imager

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<th>LDPI Evaluation</th>
<th>0 week</th>
<th>2 weeks</th>
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<td>CA-NP-1 (NP7)</td>
<td>0.73</td>
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<td>0.54</td>
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NP7(Caffeoyl-NP-1)

Clinical Data of NP7

Volunteer: HHS

0 week (Before)

2 weeks (After)

NP7 Containing Cream

CA-NP-1 (NP7)

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<tr>
<th>LDPI Evaluation</th>
<th>0 week</th>
<th>2 weeks</th>
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<td>NP7 Containing Cream</td>
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<td>CA-NP-1 (NP7)</td>
<td>0.85</td>
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Improvement of Blood Circulation on Atopic dermatitis by Laser Doppler Perfusion Imager
Clinical Data of NP7

Volunteer: HSH

NP7 Containing Cream

CA-NP-1 (NP7)

Improvement of Blood Circulation on Atopic dermatitis by Laser Doppler Perfusion Imager

<table>
<thead>
<tr>
<th>LDPI Evaluation</th>
<th>0 week</th>
<th>2 weeks</th>
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<td>NP7 Containing Cream</td>
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<td>0.50</td>
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<td>CA-NP-1 (NP7)</td>
<td>0.76</td>
<td>0.51</td>
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</table>
Clinical Data of NP7: Improvement of Blood Circulation on Atopic dermatitis by Laser Doppler Perfusion Imager

Blood Circulation Changes

- NP7 Containing Cream
- CA-NP-1 (NP7)
- Control

0 week (Before) vs. 2 weeks (After)
# Product Information

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<th>NP7</th>
<th>Manufacturer</th>
<th>BIO-FD&amp;C Co., Ltd (<a href="http://www.biofdnc.com">www.biofdnc.com</a>)</th>
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</thead>
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<td><a href="mailto:shmoh@biofdnc.com">shmoh@biofdnc.com</a></td>
<td>82-32-811-2027 Fax 82-32-822-2027</td>
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<table>
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<tr>
<th>PCPC Name</th>
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<tr>
<td>Packing Unit</td>
<td>500ppm solution type, 10Kg/packing unit</td>
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<td>Recommended Dosage in Cosmetic Formula</td>
<td>1~3%</td>
</tr>
</tbody>
</table>

## Characteristics
- Synthetic Peptide Materials (Caffeic acid coming from coffee tree in conjunction with Neuropeptide-1(sh-Octapeptide-4))
- Solubility: 1.6g / 100 ml (H2O)
- High Stability in Solution
- M.W. 1040.1 Da

## Function
- Anti-Inflammation Effect
- Anti-Irritation Effect
- Clinically good efficacy in atopic dermatitis

## IP
- Patent Title: Novel Cinnamoyl Peptide Derivative Having 4-Hydroxy Substituent, Method For Preparing The Same And Cosmetic Composition Comprising The Same.
- Registered Number 10-2008-0084159
- Country / Registered Date: KR / 2008.08.27

## References
* sh-Decapeptide-9

The INCI name of the Decapeptide-9 is changed to the sh-Decapeptide-9 by PCPC.
Structures for Neoendorphin

Chemical Formula: C_{30}H_{39}N_{12}O_{13}
Exact Mass: 1227.68
Molecular Weight: 1228.44
m/z: 1227.68 (100.0%), 1228.68 (66.4%), 1229.68 (27.4%), 1228.67 (5.5%), 1230.69 (4.7%), 1230.68 (3.1%), 1231.69 (1.3%)
Elemental Analysis: C, 58.66; H, 7.30; N, 17.10; O, 16.93

<3D Structure of Neoendorphin>
Neoendorphin is a Sort of Neuropeptide

Neoendorphin is a sort of neuropeptides which are found in neural tissue. Neuropeptides are enkephalin, neoendorphin, α-endorphin, β-endorphin, dynorphin, neurotensin, neuromedin U, and somatostatin. These peptides are all released centrally and act on other neurons at specific receptors. Peptide signals play a role in information processing that is different to that of conventional neurotransmitters, and many appear to be particularly associated with specific behaviors. For example, neoendorphin has striking and specific effects on skin retexturizing in signal communication between skin and neural system. Neuropeptide, such as neoendorphin, acts a driving force to repair scars and wrinkles, to increase production of collagen, to accelerate wound healing effect.

THE Neuropeptide Contribution to Skin Care

- Increase production of collagen
- Repair scars and wrinkles
- Increase circulation, resulting in radiance and glow
- Experience rapid wound repair
- Develop a dewy, supple appearance to skin
Neoendorphin is a Sort of Neuropeptide

The ‘beauty’ of skin neurobiology

Neoendorphin can directly bind to the kappa opioid receptor (KOR) on the plasma membrane of skin cells such as keratinocyte and fibroblast. And then it induces a variety of biological events, such as wound healing and skin retexturizing.
Neoendorphin

MTT Assay of Neoendorphin

Proliferation Effect on Human Skin Cell (HaCaT) after Treatment for 48 hrs

<table>
<thead>
<tr>
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<th>Average</th>
<th>S.D.</th>
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<tr>
<td>Control</td>
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<tr>
<td>1 nM</td>
<td>102.24</td>
<td>7.83</td>
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<tr>
<td>100 nM</td>
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<tr>
<td>1 μM</td>
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<td>5 μM</td>
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<td>10 μM</td>
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- MTT: Mitochondrial Tetrazolium Reduction
- Combination: Neoendorphin
Neoendorphin

Irritation Data of Peptides

Skin Irritation Test

1. Distilled Water (DW) as negative control
2. 10% Sodium Lauryl Sulfate (SLS) as positive control
3. Neuropeptide-1
4. Neuropeptide-2
5. α-Endorphin
6. γ-Endorphin
7. Neoendorphin
8. Met-Enkephalin
9. Caffeoyl-Neuropeptide-1
10. Gold-binding Peptide-1

(Treated Samples to Volunteers after 48hrs)
# Product Information

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Neoendorphin</th>
<th>Manufacturer</th>
<th>BIO-FD&amp;C Co., Ltd (<a href="http://www.biofdnc.com">www.biofdnc.com</a>)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact</td>
<td>Sang Hyun Moh</td>
<td>Contact</td>
<td>Sang Hyun Moh <a href="mailto:shmoh@biofdnc.com">shmoh@biofdnc.com</a></td>
</tr>
<tr>
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<td>Phone</td>
<td>82-32-811-2027 Fax 82-32-822-2027</td>
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<td>PCPC Name</td>
<td>sh-Decapeptide-9</td>
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<td>Packing Unit</td>
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<td>Recommended Dosage in Cosmetic Formula</td>
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<td>Characteristics</td>
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<td>Solubility : 3g / 100 ml (H2O)</td>
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<td>High Stability in Solution</td>
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<td>M.W. 1228.4 Da</td>
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<td>Anti-inflammatory Cosmetic Composition for Wound healing and tissue Regeneration.</td>
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Derma-Lucia Skinceuticals LLC

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