SPIRAEA EXUDACTIVE®
for High skin hydration
Extract from Spiraea ulmaria
First active in PAT’s collection
OVERVIEW

• Spiraea Exudactive®
  short story
• Biological efficacy
• Cosmetic application
• Technical information
• Ask for more!
Spiraea Exudactive®
short story
The Queen of the Meadow, Rosaceae family, perennial herb with large leaves and beautiful white flowers grouped in clusters. Mostly found in Europe, the meadowsweet was a sacred plant for druids. The whole plant was once eaten as a condiment. Leaves, flowers and roots of *Spiraea ulmaria* were used in traditional pharmacopoeia, especially for its content in salicylic acid well-known for its analgesic effects, and in acetylsalicylic acid used for a long time as the active ingredient in aspirin.
Biological efficacy

Objectivation of the extract
  Full genome analysis
  Protein quantification
  Functionnal assay
  Clinical trial
  Efficacy results in brief
Full objectivation was carried out from full genome analysis to *in vivo* evaluation, to evaluate the potential of Spiraea Exudactive® product and prove the cosmetic activities.

Objectivation steps:

1. **Full Genome Analysis**
   - Hypothesis
2. **Protein Quantification**
   - Proof of expression
3. **Functional Assay**
   - In vitro activity
4. **Clinical Trial**
   - In vivo activity
BIOLOGICAL EFFICACY

Efficacy Results

Gene Cluster Involved in Hydration

- incl. Aquaporin-3 (AQP3) (x3.5)
- Caspase 14 (CASP) (x8.7), ATP Binding Cassette receptor (ABCA12) (x2.1)

Gene Cluster Involved in Skin Barrier Function, in particular the components of the desmosomes

- incl. Desmoglein-1 (DSG1) (x23.8)
- Claudine-1 (CLDN1) (x3.1)

Genes positively modulated by Spiraea Exudactive® on keratinocytes (NHEKs):

Potential activity of Spiraea Exudative® in epidermal cohesion, limitation of water loss and improvement of hydration
Desmoglein-1 (DSG1) is a transmembrane glycoprotein, main constituent of Desmosomes. Its increase is correlated with a reinforcement of skin barrier function.

In green = expression of target gene

Legend:
*: significant, **: highly significant, ***: very highly significant
**Immunostaining of Claudin-1 on keratinocytes – T=72h**

Claudin-1 (CLDN1) is a membrane protein, main constituent of tight junctions. Its increase is correlated with a reinforcement of skin barrier function.

In keratinocyte cultures, Spiraea Exudactive® (0.1 - 0.05 - 0.025%) significantly increases the abundance of two markers of tight junction and desmosomes, namely claudin-1 and desmoglein-1.
Aquaporin-3 (AQP3) is a membrane protein playing a key role in hydration control. Its increase is correlated with a better hydration of the skin.
Caspase-14 (CASP-14) is an enzyme responsible for the degradation of profilaggrin into filaggrin, which is furthermore degraded in Natural Moisturizing factor (NMF). The over expression of Caspase 14 is therefore linked to an hydration effect.
ABCA12 is a transmembrane protein that actively acts for the transfer of lipids in the stratum corneum. Its overexpression reinforces the barrier function of the skin and its hydration.

- The transcriptomic data previously obtained by full genome analysis are confirmed by Real-Time qRT-PCR.

- Strong potential of Spiraea Exudactive® extract on the barrier function of the epidermis and in particular on the maintenance of the stratum corneum hydration.

- Important role in the differentiation of keratinocytes and potentially in the stratification of the epidermis by targeting specific markers of each of these layers.

- Remarkable dose effect between several concentrations tested.
The morphology of the tissues was verified after histological staining of the epidermis. The transepidermal electrical resistance (TEER) can be measured at 4 non-cytotoxic concentrations.
BIOLOGICAL EFFICACY

EFFICACY RESULTS

3 | FUNCTIONAL ASSAY

IN VITRO ACTIVITY

→ Effect on the barrier function - TEER results on in vitro reconstituted epidermis (RHEs) - treated during 10 days

TEER (Trans epidermal electrical resistance): TEER measurement allows to evaluate the efficiency of the epidermal barrier function, essential to ensure the moisturizing of the superficial layers of the skin. A higher resistance = more cohesive, low permeability structure so more hydration.

→ Spiraea Exudactive® increases remarkably the barrier function of the treated epidermis, relative to the solvent, with a dose dependent effect.

→ The best Trans epidermal electrical resistance is observed at the highest concentration.

→ This functional test, evaluating the overall barrier function of the epidermis, demonstrates that Spiraea Exudactive® significantly increases transdermal electrical resistance (TEER) of treated epidermis.
**BIOLOGICAL EFFICACY**

**EFFICACY RESULTS**

### 4 | CLINICAL TRIAL

**IN VIVO ACTIVITY**

- **Corneometer® results during 14 days**

![Graph showing moisture increase over 14 days]

- Significant increase of humidity level
- **Long-term moisturizing** of superficial epidermal layers
- **60% more moisturized skin** applying Spiraea Exudactive® active formula during 14 days compared to placebo

- **Cosmetic formulation**: Body milk formulated with 1.5% of the active

- **Protocol**: Single blind study on 21 female subjects, twice daily application, active formula vs placebo

- **High and long-lasting moisturizing effect**
BIOLOGICAL EFFICACY

EFFICACY RESULTS

4 | CLINICAL TRIAL

IN VIVO ACTIVITY

➔ Tewameter® results during 14 days

➔ Natural water loss radically decreases thanks to the active formula
➔ The action of placebo stabilizes at D7 whereas the active formula continues moisturizing the skin during 14 days
➔ 52% more efficacy observed at D14 compared to placebo

➔ Skin barrier improved and high regulation of skin water balance

➔ Spiraea Exudative® presents moisturizing and protective effects after 7 and 14 days of use compared to placebo. The product globally improves skin hydration and strengthens barrier in the long run.
SPIRAEA EXUDACTIVE®, A GLOBAL MOISTURIZER AND SKIN BARRIER ENHANCER

→ Full objectivation with fantastic results
→ Moisturizing cosmetic applications demonstrated through a global mechanism of actions: abundance of major constituents of the cellular junctions and on the overall barrier function of the epidermis
COSMETIC APPLICATIONS

Cosmetic activities
Formulation advice
Innovative process of production
COSMETIC APPLICATIONS

COSMETIC ACTIVITIES & FORMULATION

COSMETIC ACTIVITIES

→ Novel active ingredient with outstanding moisturizing claims
  → More hydrated skin
  → Stronger epidermal barrier
  → Better cohesion of skin cells
  → Skin water balance recovered
  → Long lasting effects

FORMULATION ADVICE

Recommended dose between 1% to 3%

Solubility: water-soluble
COSMETIC APPLICATIONS

INNOVATIVE PROCESS OF PRODUCTION

PAT Plant Milking® technology for sustainable exploitation of root content

1. Choice of the plant species
   - Even rare ones

2. Supply and multiplication

3. Soil-free cultivation (aeroponics) in greenhouses and exploitation of the roots

4. Stimulation of the production of molecules, up to 50 fold increase

5. Molecular root exudation of living plants - 3 to 8 yearly harvests on the same plants

6. Finalization

Patent WO0133942

“PAT Plant Milking®” INPL - INRA – exclusive world-wide license

Specific flowchart available for Spiraea Exudactive®
COSMETIC APPLICATIONS

INNOVATIVE PROCESS OF PRODUCTION

Industrial production

Biodiversity

Access to roots, even from trees
COSMETIC APPLICATIONS

INNOVATIVE PROCESS OF PRODUCTION

- Unique extraction from living plants vs dead plants
- Traceability: From seeds to active in one location
- Outstanding consistency and yield
- Few thousands selected plants to cover worldwide needs
- Allowing « unsourceable » sourcing...
TECHNICAL INFORMATION

Toxicological results
Technical data
Specifications
No toxicology observed on Spiraea Exudactive®

Detailed toxicological tests carried out:

- Het-Cam test
- Skin irritation on NHEKs (OECD 439)
- 3T3 NRU in-vitro phototoxicity (OECD 432)
- Ames test (OECD 471)
- In-vitro sensitization (OECD 442D)
- Evaluation of existing toxicological data
- Evaluation of sensitizer potential and cutaneous compatibility on volunteers (MARZULLI-MAIBACH method)
## TECHNICAL INFORMATION

### TECHNICAL DATA

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product name</strong></td>
<td>SPIREA EXUDACTIVE®</td>
</tr>
<tr>
<td><strong>Manufacturer</strong></td>
<td>Plant Advanced Technologies PAT SA, France</td>
</tr>
<tr>
<td><strong>Plant species</strong></td>
<td><em>Spiraea ulmaria</em> (root part)</td>
</tr>
<tr>
<td><strong>Production process</strong></td>
<td>living root exudation thanks to PAT plant milking ® technology</td>
</tr>
</tbody>
</table>

### COMPOSITION & ORIGIN

<table>
<thead>
<tr>
<th>Ingredient/INCI name</th>
<th>PROPANEDIOL, SPIRAEA ULMARIA ROOT EXTRACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antioxidants, Preservatives</td>
<td>CITRIC ACID (77-92-9 / 5949-29-1)</td>
</tr>
<tr>
<td><strong>CAS number</strong></td>
<td>504-63-2 / 26264-14-2, 84775-57-5</td>
</tr>
<tr>
<td><strong>EINECS number</strong></td>
<td>207-997-3, 283-886-3, 201-069-1</td>
</tr>
<tr>
<td><strong>Raw material origin</strong></td>
<td>vegetable, France</td>
</tr>
<tr>
<td><strong>Nagoya status</strong></td>
<td>Compliant (origin plant source in Germany)</td>
</tr>
</tbody>
</table>

### TRADE INFORMATION

<table>
<thead>
<tr>
<th>IECIC listed</th>
<th>SPIRAEA ULMARIA EXTRACT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Application patent</strong></td>
<td>#FR1770000022</td>
</tr>
<tr>
<td><strong>Trademark</strong></td>
<td>Spiraea Exudactive® is a French registered trademark of PAT SA #16 4 278 781</td>
</tr>
</tbody>
</table>
### SPECIFICATIONS

<table>
<thead>
<tr>
<th>ORGANOLEPTIC PROPERTIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspect</td>
</tr>
<tr>
<td>Odor</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PHYSICO-CHEMICAL PROPERTIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent content (% w/w) (1,3-Propanediol)</td>
</tr>
<tr>
<td>Dry extract (g/kg)</td>
</tr>
<tr>
<td>pH of the extract</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MICROBIOLOGICAL PROPERTIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target pathogens</td>
</tr>
<tr>
<td>Aerobic mesophilic bacteria /g</td>
</tr>
<tr>
<td>Yeast-fungi / g</td>
</tr>
<tr>
<td>Escherichia coli / g</td>
</tr>
<tr>
<td>Staphylococcus aureus / g</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa / g</td>
</tr>
<tr>
<td>Candida albicans / g</td>
</tr>
<tr>
<td>Streptocoques D group / g</td>
</tr>
</tbody>
</table>
ASK FOR MORE!

PAT at a glance
Spiraea Exudactive® & more products
ASK FOR MORE!

PAT AT A GLANCE

- Founded in 2005 - Specialist of the identification, optimization, and production of rare biomolecules from plants

- Large Research and Production capacities - 3 Ha of Greenhouse

- A team of 40 people, half dedicated to R&D

- Euronext Growth ® (former Alternext market) since 2015. Approx. 4,000 individuals shareholders. Founders still own 51% equity. Over 10M€ raised capital.

- Over 30 patents and dozen of trademarks

- ISO 9001 certification since 2015

- PAT Group: StratiCELL (in-vitro tests), PAT Zerbaz (aeroponic greenhouses in Reunion island) and Couleurs de Plantes (natural pigments & colorants)
ASK FOR MORE!
SPIRAEA EXUDACTIVE® & MORE PRODUCTS

More about Spiraea Exudactive®

• More details, methodology and technical documentation available for Spiraea Exudactive® on demand

• Samples available on demand

More products to come

• PAT is newly developing a collection of Exudactive - Spiraea Exudactive® is the first one

• PAT proposes custom-made development of active extracts through PAT plant milking® - Ask PAT SA for a presentation
PAT plant milking®
Source the unsourcable!

Anne MUSCI-CARISSIMO
International Sales Manager
Plant Advanced Technologies PAT
France

sales@plantadvanced.com
www.plantadvanced.com
Tél. : +33 (0)3 83 94 03 42