Recent Technology and Products for Anti-Hair Loss
Hair Loss Treatment Market

**Global Market size for 5 years**

- World
- Asia Pacific
- North America
- Western Europe
- Latin America

**Market size in 2011**

- Japan: 423.7 US $ mn
- USA: 119.4 US $ mn
- France: 20.3 US $ mn
- China: 13.9 US $ mn
- Korea: 13.6 US $ mn
- Germany: 11.4 US $ mn
- United Kingdom: 8.9 US $ mn

* US $ mn
* Euromonitor, Category Definition:
- Includes only those which restore or correct hair loss, excluding cosmetics

**Estimation the size of Anti-hair loss market in Korea**

- **Pharmaceuticals**: 40 mn $ (20%)
- **Salon**: 40 mn $ (20%)
- **Cosmetics**: 160 mn $ (80%)

[ Evolution of Scalp care market in Korea ]

Self care → Receiving scalp & hair treatment in Salon
Anti-hair loss + Head Spa Market size is estimated 2 bn $.
Market of Scalp care products is 200 mn $.

[cosmetics +Quasi-drugs 80% : Pharmaceutical products 20%]
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Causes and Featured Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Androgenetic Alopecia</td>
<td>The leading cause of bald (genetic reason, testosterone)</td>
</tr>
<tr>
<td>Alopecia Areata</td>
<td>Causes bald spots on scalp, or spread to the entire scalp. (Alopecia Totalis)</td>
</tr>
<tr>
<td></td>
<td>Autoimmunity defect by stress</td>
</tr>
<tr>
<td></td>
<td>Can be cured by continuous treatment</td>
</tr>
<tr>
<td>Postpartum Telogen Effluvium</td>
<td>A reactive process caused by a metabolic or hormonal stress</td>
</tr>
<tr>
<td></td>
<td>A form of hair loss where more than normal amounts of hair fall out</td>
</tr>
<tr>
<td>Endocrine Disorder</td>
<td>Malfunction of hypothalamus, hypothyroidism, diabetes</td>
</tr>
<tr>
<td>Nutrition Lesion, Disturbances</td>
<td>Disorder of nutrition</td>
</tr>
<tr>
<td>of metabolism</td>
<td></td>
</tr>
<tr>
<td>Medical Substances</td>
<td>Anticancer drug</td>
</tr>
<tr>
<td></td>
<td>Suppression of germinal matrix division</td>
</tr>
<tr>
<td>Traumatic Alopecia</td>
<td>Induced by physical trauma.</td>
</tr>
<tr>
<td></td>
<td>Traction, Pressure, Tricotillomania(mental illness)</td>
</tr>
<tr>
<td>Skin disease</td>
<td>External factor : parasite, worm,</td>
</tr>
<tr>
<td></td>
<td>Internal factor : food, drugs, blood vessel system</td>
</tr>
<tr>
<td></td>
<td>Sectional pruritus : alopecia seborrheica, dandruff</td>
</tr>
<tr>
<td>Cicatricial Alopecia</td>
<td>Chemical exogenic reasons (acid, alkali), Physical exogenic reasons (radiation)</td>
</tr>
</tbody>
</table>
Miniaturizing Process of Hair Bulb in Androgenetic Alopecia

(TRENDS in Molecular Medicine Vol.7 No.7 July 2001)
The Metabolism of Male Sex Hormone

Dehydroepiandrosterone-Sulfate (DHEA-S)

STS

Dehydroepiandrosterone (DHEA)

Androstenediol

3α-HSD/Δ^5→4 isomerase

17β-HSD

Testosterone (T)

5α-Reductase

Dihydrotestosterone (DHT)

3α-HSD

5α-Reductase

Androstenedione

Androsterone

3α-Androstanediol glucuronid

Glucuronidase

Androstarone-glucuronid

17β-Estradiol

3α-Androstanediol

3β-HSD/Δ^5→4 isomerase

Estrone

STS

The Mechanism of Propecia (medicine)

![Diagram of the mechanism of Propecia](image)

1. **Testosterone**
2. **Finasteride**
3. **17-HSD**
4. **4-androstene-3,17-dione**
5. **5α-reductase**
6. **DHT**
7. **3-HSD**
8. **5α-androstanediol-3α,17β-diol**
9. **3-HSD**
10. **Androstanedione**
11. **5α-reductase**
12. **Androstenedione**
13. **Androsterone**
14. **Polar metabolites**
Target Parameters of Anti-Hair Loss Treatment by Regulating Hair Cycle

Hair shaft formation signals:
- BMP
- VEGF
- Wnt
- Notch, etc.

Transition signals to Catagen:
- TGF-β1
- TGF-β2
- FGF-5
- Hairless
- VDR, etc.

Transition signals to Anagen:
- FGF-7
- HGF
- IGF-1
- FGF-18
- Shh
- Wnt, etc.

BMP  Bone Morphogenetic Protein
VEGF  Vascular endothelial Growth Factor
FGF  Fibroblast Growth Factor
HGF  Hepatocytel Growth Factor
IGF  Insulin Growth Factor
TGF  Transforming Growth Factor
Research Trend of Anti-Hair Loss and Related Products

**Stimulation of**

- **FGF-7** (adenosine; Shiseido),
- **BMP-2** (benzyl aminopurine; Lion)

**Suppression of**

- **FGF-5** expression (Kao)

**Inhibition of androgen**

- 5α-Reductase inhibitor (Finasteride)
- TGF-beta suppressor (Morus root extract, Sophora extract)

**Proliferation of**

- Dermal papilla cells
  - IGF-1, IGFBP-3, HGF

**Modulation of Curling**

- Ethnic Hair (Loreal)

**Anti-Graying**

- MITF upregulation (Shiseido)
- Anti-apoptosis (Bcl-2; Loreal)
- TRP-2 upregulation (Loreal)

**Stimulation of VEGF**

- Minoxidil foam (J&J)
- Adenosine (Shiseido)
- Evolvulus alsinoides extract (POLA)
# Claimed Points and Effective Ingredients of Anti-Hair Loss Products

## 1. Stimulation of Blood Circulation

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Product</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minoxidil</td>
<td>Regaine, Rogaine, RiUP, Minoxil,</td>
<td>Pharmacia &amp; Upjohn, Hyundai pharm, hanmi pharm</td>
</tr>
<tr>
<td>Pyrimidine-3-N-Oxide Derivatives</td>
<td>Aminexil</td>
<td>L'oreal</td>
</tr>
<tr>
<td>Dialkylmonoamine Derivatives</td>
<td>藥用 紫電改 Z</td>
<td>Kanebo</td>
</tr>
<tr>
<td>Vitamin E acetate</td>
<td>Karoyan, Success Tonic, 藥用毛髮力 M power</td>
<td>Kao, Lion, Jeil Pharm.</td>
</tr>
<tr>
<td>Swertiall</td>
<td>Karoyan, Success Tonic, 藥用毛髮力 M power</td>
<td>Kao, Lion, Jeil Pharm.</td>
</tr>
<tr>
<td>Nicotinic acid amide</td>
<td>藥用 不老林 Live ACT</td>
<td>Shiseido, LG</td>
</tr>
<tr>
<td>Benzyl nicotinate</td>
<td>藥用 不老林 Live ACT, 藥用 紫電改 Z, Mo &amp; Moa</td>
<td>Shiseido, Lion, LG</td>
</tr>
<tr>
<td>Dialkylmonoamine Derivatives</td>
<td>藥用 紫電改 Z</td>
<td>Kanebo</td>
</tr>
<tr>
<td>Sophora</td>
<td></td>
<td>Shiseido</td>
</tr>
<tr>
<td>Staphylea bimalda extract</td>
<td>Success hair active</td>
<td>Kao</td>
</tr>
<tr>
<td>Pantothenyl ethylether</td>
<td>藥用 不老林 Live ACT RADKAM</td>
<td>Shiseido</td>
</tr>
<tr>
<td>Adenosine</td>
<td>Adenogen, Adenogengracy</td>
<td>Shiseido</td>
</tr>
<tr>
<td>t-flavanone</td>
<td>Success Tonic, Segreta scalp essence</td>
<td>Kao</td>
</tr>
</tbody>
</table>

## 2. Regulation of Testosterone

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Product</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finasteride</td>
<td>Finasteride</td>
<td>Merk</td>
</tr>
<tr>
<td>Eugenyl glucoside</td>
<td>藥用紫電改 Z</td>
<td>Kanebo</td>
</tr>
<tr>
<td>Sophora flavescens Aiton extract</td>
<td></td>
<td>LG</td>
</tr>
</tbody>
</table>

## 3. Activation of Dermal Papilla Cell

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Product</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentadecaglyceride (PDG)</td>
<td>藥用毛髮力 M power</td>
<td>Kanebo</td>
</tr>
<tr>
<td>Hinokitiol</td>
<td></td>
<td>RADKAM</td>
</tr>
<tr>
<td>Pyridoxine HCL(Vit. B6)</td>
<td>RADKAM</td>
<td></td>
</tr>
<tr>
<td>D-panthenol</td>
<td>藥用紫電改 Z</td>
<td>Kanebo</td>
</tr>
</tbody>
</table>

## 4. Scalp moisturization

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Product</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>paeonia suffruticosa extract</td>
<td>藥用 不老林 Live ACT</td>
<td>Shiseido</td>
</tr>
<tr>
<td>cuachalalate (juliania adstringent) extract</td>
<td>藥用 不老林 Live ACT</td>
<td>Shiseido</td>
</tr>
<tr>
<td>Coleus extract</td>
<td>藥用毛髮力 M power</td>
<td>Liom</td>
</tr>
<tr>
<td>Biofluorine</td>
<td>kearastase biotic</td>
<td>Loral</td>
</tr>
<tr>
<td>Coix extract</td>
<td>Mo &amp; Moa</td>
<td>LG</td>
</tr>
</tbody>
</table>
Research flow of AmorePacific
Research Method

The Selection of Candidate Material

Refer to the Oriental traditional medical book and folk remedies
Ex) Donguibogam, Korean traditional medical book

- Biological Effects
  - Evaluation of specific traditional medicinal plants
  - Searching for novel mechanism

- Clinical Evaluation
  - Evaluation of real effect in human test
  - Sensory test

- Physical Properties
  - Tensile strength using tress (or human hair)
  - Shininess, cortex smooth, color appearance

- Stabilization
  - Increasing the stabilities of natural ingredients
  - Searching for stabilizing agents

- Mildness Test
  - Searching for mild surfactants
  - Evaluation of mildness in formulation
Previous Study Results

Activity evaluation of *Thujae occidentalis* semen (TOS) extract

- In our search for 5α-reductase inhibitor from oriental medicinal plants (340 species), we found that the extract of *Thujae occidentalis* semen (TOS) is effective for inhibition of 5α-reductase.
- The leaves and the fruits of *Thujae occidentalis* have been known as well to serve as an oriental herbal medicine for the treatment of renopathy, leukotrichia and alopecia.

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC	extsubscript{50} values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic acid</td>
<td>31.55µg/ml</td>
</tr>
<tr>
<td>γ-Linoleic acid</td>
<td>5.55µg/ml</td>
</tr>
<tr>
<td>TOS extract</td>
<td>2.6µg/ml</td>
</tr>
</tbody>
</table>

A : testosterone  
B : testosterone + vehicle  
C : testosterone + 5% cyproterone acetate (CA)  
D : testosterone + 1% TOS extract
Previous Study Results

**Clinical test (total 40 volunteers)**

- 20 people used APHG-0803 shampoo (including TOS extract) and the other 20 people used control shampoo once in a day
- For the base line, hairs on the transitional zone was shaved (1.5cm in diameter)
- Shed hair count, phototrichogram parameters (total hair count, anagen/telogen ratio)
- Statistical analysis: wilcoxon signed-rank test or two sample T test

<table>
<thead>
<tr>
<th>Total Hair Counts</th>
<th>Fallen Hair Counts</th>
<th>Terminal Hair Counts</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Graph" /></td>
<td><img src="image2" alt="Graph" /></td>
<td><img src="image3" alt="Graph" /></td>
</tr>
</tbody>
</table>

Change rate (%)

- 8wks
- 16wks

- APHG-0803
- Control

p=0.009
p=0.017
p=0.044
Approach Method

1st TOS

5α-Reductase

2nd Scutellaria Baicalensis Georgi and Glycyrrhiza Glabra L

Growth Factor

Next Target

Cell Membrane

Nuclear Membrane

Physiologic effect

Anagen-to-catagen transition
Proliferation ceases
Apoptosis begins in bulb/ORS
Differentiation ceases

Catagen regression phase
Differentiation ceases

Telogen-to-anagen transition
Stem cells activated
Cells near DP proliferate

The Hair Cycle
Laura Alonso and Elaine Fuchs
**Approach Method**

### Verification of Anti-Hair Loss Effects (in vitro)

<table>
<thead>
<tr>
<th>Categories</th>
<th>Assay List</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth Factors assay</td>
<td>▪ Stimulation of IGF</td>
</tr>
<tr>
<td></td>
<td>▪ Suppression of EGF</td>
</tr>
<tr>
<td></td>
<td>▪ Suppression of TGF-β</td>
</tr>
<tr>
<td></td>
<td>▪ Stimulation of FGF</td>
</tr>
<tr>
<td>Anti-androgen effect</td>
<td>▪ Inhibition of Androgen Receptor</td>
</tr>
</tbody>
</table>

**The usage in Oriental traditional medical book**

<table>
<thead>
<tr>
<th><strong>Scutellaria baicalensis Georgi</strong></th>
<th>Scutellaria baicalensis Georgi (SBG) is the representative traditional plant for the treatment of inflammation, anti-oxidant and alopecia. In oriental medicine, its property is cold and it is believed that SBG extract can bring down fever (anti-inflammation)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glycyrrhiza glabra L.</strong></td>
<td>Licorice (Glycyrrhiza glabra L., GGL) is also frequently used in traditional medicine to treat inflammatory and allergic diseases and widely used in pharmaceutical. Especially dipotassium glycyrrhizinate originated from licorice is very famous for alopecia</td>
</tr>
</tbody>
</table>
Experimental Results

Biological Effects of *Scutellaria baicalensis* Georgi (SBG)

- The androgen receptor is an intracellular steroid receptor that specifically binds testosterone and dihydrotestosterone. Flutamide is used as a positive control and SBG extract is the effective inhibitor of androgen receptor. Baicalin, which is the main component of SBG, also can decrease the binding affinity dose-dependently.

**<DPC proliferation Assay>**

<table>
<thead>
<tr>
<th></th>
<th>control</th>
<th>2 ppm</th>
<th>5 ppm</th>
<th>1 ppm</th>
<th>2 ppm</th>
<th>5 ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baicalin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**<Androgen Receptor Inhibition Assay>**

- Flutamide inhibits the androgen receptor.
- SBG extract is effective in inhibiting the androgen receptor.
- Baicalin also inhibits the androgen receptor.

- The androgen receptor is an intracellular steroid receptor that specifically binds testosterone and dihydrotestosterone. Flutamide is used as a positive control and SBG extract is the effective inhibitor of androgen receptor. Baicalin, which is the main component of SBG, also can decrease the binding affinity dose-dependently.
Experimental Results

Biological Effects of *Glycyrrhiza glabra* L. (GGL)

- Transforming growth factor (TGF-β) plays important roles in the induction of catagen during the hair cycle. Licorice (*Glycyrrhiza glabra* L., GGL) extract can effectively suppress TGF-beta action.
- Production of Fibroblast growth factor (FGF) is increased by GGL extract, especially it showed the highest activity at 10ppm, respectively.

<Inhibition of TGF-β>

<Activation of basic-FGF>
Anti-Hair Loss Quasi-Drug of Amorepacific: 뮐 (Ryo)

- Shampoo
- Scalp & Hair Pack
- Scalp Essence
Clinical Results of 류(Ryo) Anti-hair loss shampoo

Clinical Evaluation Methods

- 40 volunteers, four-block randomized
- 20 people used RJ shampoo and the other 20 people used control shampoo once in a day
- For the base line, hairs on the transitional zone was shaved (1.5cm in diameter)
- Shed hair count, phototrichogram parameters (total hair counts and hair diameter)

Volunteers Information

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Age (year)</th>
<th>Total Hair Counts (N/cm²)</th>
<th>Hair Diameters (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20.00</td>
<td>41.65</td>
<td>100.60</td>
<td>0.068</td>
</tr>
<tr>
<td>RJ group</td>
<td>20.00</td>
<td>42.05</td>
<td>110.11</td>
<td>0.063</td>
</tr>
</tbody>
</table>

Phototrichogram evaluation

1. Total hair count (number/cm²)
2. Hair diameter (mm)

Shampoo Formulation

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Control</th>
<th>RJ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deionized water</td>
<td>To 100</td>
<td>To 100</td>
</tr>
<tr>
<td>Ammonium lauryl sulfate (25%)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Zinc pyrithione (48%)</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>SBG extract</td>
<td>-</td>
<td>0.1</td>
</tr>
<tr>
<td>GGL extract</td>
<td>-</td>
<td>0.1</td>
</tr>
<tr>
<td>Ammonium lauryl ether sulfate (25%)</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Soyamidopropyl amine oxide (25%)</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Polyquaternium 10</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>EDTA 2Na</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Phenoxyethanol</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Fragrance</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Clinical Results of 류(Ryo) Anti-hair loss shampoo

Phototrichogram results

- The results of phototrichogram analysis showed that the total hair count and hair diameter of RJ group (test group) increased respectively.
- The RJ group showed great effect compared to control group respectively.

**Total Hair Counts (number/cm²)**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>RJ (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20w</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Hair Diameter (mm)**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>RJ (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20w</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Phototrichogram results showed that:
- The total hair count and hair diameter of RJ group increased.
- The RJ group showed greater improvement compared to the control group.
Clinical Results of 変(Reo) Anti-hair loss shampoo

Clinical photography results
- The clinical photography shows that the hair density of RJ group increased compared to control group respectively.
Clinical Results of 〦(Ryo) Anti-hair loss shampoo

Comparison of self-sensory affirmative evaluations

- **Improvement of vertex hair**: 8 weeks (Control), 16 weeks (RJ)
- **Improvement of frontal hair line**: 8 weeks (Control), 16 weeks (RJ)
- **Improvement of hair thickness**: 8 weeks (Control), 16 weeks (RJ)
- **Improvement of hair growth**: 8 weeks (Control), 16 weeks (RJ)
- **Reduction in hair loss**: 16 weeks (Control), 8 weeks (RJ)
Clinical Results of 뮼 (Ryo) Scalp & Hair Pack

Clinical test results

(a) Decrease the number of fallen hair
(b) Increase hair diameter
(c) Increase rate of hair growth

(A) Measurement of the temperature of skin by LDI (laser Direct Imaging),
(B) Imaging of skin that before and after treatment of Ryo scalp & hair pack by IR imaging camera.

(a) Before treatment,
(b) directly after the treatment of Ryo scalp & hair pack
and wash-off,
(c) 10 minutes after the treatment.
1. Recently, various effects of Korean traditional medicinal plants are studied in the field of hair-care product.

2. In the previous study, *Thuja occidentalis* semen extract showed an inhibitory effect on human 5α-Reductase and also showed retardation of hair loss in 16 weeks clinical test.

3. *Scutellaria baicalensis* Georgi and *Glycyrrhiza glabra* L. can control the growth factors related to hair-loss and be the regulators of Androgen Receptor.

4. *Scutellaria baicalensis* Georgi and *Glycyrrhiza glabra* L. showed anti-hair loss effects in clinical tests.

5. Anti-hair loss quasi-drugs and cosmetics related with scalp care are increasing, and types of products will be highly diversifying.
THANK YOU

AMOREPACIFIC