Epidermal Growth Factor \textbf{DW-EGF} 

borned in the exclusive bio-technology of Daewoong Pharma.
1. What is EGF?
   - EGF
   - EGF and skin aging

2. The start of Easydew
   - started as pharmaceuticals

3. DW-EGF development evolution
   - Epidermal Growth Factor (EGF)

4. DW-EGF in Easydew
   - WHO registration, global standard EGF

# attachment_EGF thesis
1. What is EGF? Epidermal Growth Factor

- Single-chain, non-glycosylated protein (6,200 daltons with 53 amino acids)

- Trace of EGF is detected in body fluid, such as breast milk, urine, saliva, tear etc.

- Regarded as an endogenous healing factor of skin, corneal and intestinal, mucosal wounds

- It enforces cell division that leads to proliferation of Keratinocyte and Fibroblast that synthesizes ECMs such as collagen and elastin.
1. What is EGF?  Epidermal Growth Factor

# EGF efficacy

**Regeneration**
Regenerating the skin by stimulating new skin cells and minimizing the skin wound

**Wrinkle improvement**
Stimulating the division of Fibroblast which synthesizes collagen and elastin

**Hydration**
Enhancing the skin barrier and moisturizing the skin

**Pigmentation prevention**
Preventing the melanin and tyrosinase during the wound-healing process

**Angiogenesis**
Induction of angiogenic factors

EGF’s various effects on the skin
Proliferation and migration of epithelial cells by EGF
1. What is EGF?

After 29 years-old, endogenous EGF is quickly decreased along with skin aging.
2. The start of Easydew started as pharmaceuticals

The birth of Easydew,

It is born from the special medicine EasyF external liquid (core component: EGF), which is used for diabetic foot ulcer treatment.

Not only for diabetic foot ulcer treatment, but also for continuous care and prevention, Daewoong pharma. started to develop cosmetics after getting known the importance of EGF. Combined with the advanced genetic technologies and the know-how from aesthetic experts, Easydew was launched in 2006.

* Easydew is an special brand for hospitals created by Daewoong Pharmaceutical and DNCompany
3. DW-EGF Development Evolution

- 1984: shEGF development approved
- 1987: First genetics license obtained
- 1997: First clinical trial for diabetic foot ulcer
- 1998: Second clinical trial for diabetic foot ulcer
- 2001: EasyF external liquid launched (new biopharmaceuticals No. 1)
- 2005: CELLISYS launched
- 2006: EASYDEW launched
- 2008: WHO INN (Nepidermin) obtained
- 2009: EASYHAIR (pilatory) license obtained
- 2010: EASYF Ointment launched
4. DW-EGF in Easydew

**The first EGF medicine**

- DW-EGF was used to develop the world-first EGF medicine by Daewoong Pharmaceutical with its innovative technology
- DW-EGF has obtained 34 patents in 23 countries

**WHO INN obtained**

- The only one that obtained WHO INN
  - WHO INN: Nepidermin
  - CAS No: 62253-63-8
  - WHO Drug Information (2008), 22(1):59

**The first EGF in ICID**

- DW-EGF is the world-first ingredient registered in International Cosmetic Ingredient Dictionary (ICID), 2002 9th Edition

**Various treatment**

- Diabetic foot ulcer (2001)
- Anti-wrinkle cosmetics (2005)
- Moisturizing cream (2006)
- Hair tonic (2009)
- skin wound (2010)
- chemotherapy-radiation induced oral mucositis (P3)
4. DW-EGF in Easydew

The highest purity

- DW-EGF has the high purity of 99.5% which is the medicine grade

The same structure with Human EGF

- The analysis shows that DW-EGF has the same structure with the human EGF in urine

Analysis on the structure of Human EGF in urine and DW-EGF (CD spectrum)
4. DW-EGF in Easydew  What makes it different?

- Efficacy of DW-EGF

- **Wound healing**
  
  Recover the damaged skin and repair the scar

- **Skin regeneration**
  
  Promote cell generation and increase skin energy

- **Wrinkle reduction**
  
  Promote collagen formation and enhance skin elasticity

Various efficacy of DW-EGF that proved by several clinical trails
4. DW-EGF in Easydew WHO Certification

Daewoong Pharma. has succeeded in the development of EGF which has the same structure with human EGF by its innovative technology.

DW-EGF is a pharmaceutical-grade ingredient and has obtained the WHO certification with an International Nonproprietary Name (INN) as Nepidermin.

The world-first WHO certification

There was no previous case that pharmaceutical ingredient obtained an INN among Korean Pharmaceuticals. And DW-EGF from Daewoong Pharma. is the first one obtaining INN as Nepidermin, which was made according to the regulation of WHO INN Guide Line.

New + epithelialization + dermin

<table>
<thead>
<tr>
<th>nepidermin</th>
<th>human epidermal growth factor, recombinant DNA origin epidermal growth factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>nepidermin</td>
<td>facteur humain de croissance épidermique, origine ADN recombinante facteur de croissance épidermique</td>
</tr>
<tr>
<td>nepidermine</td>
<td>factor de crecimiento epidérmico humano, origen: ADN recombinante factor de crecimiento epidérmico</td>
</tr>
</tbody>
</table>

Proposed INN: List 07
4. DW-EGF in Easydew  The world-first ICID registration

- The world-first EGF registered in ICID

DW-EGF is the first one that has been registered in ICID as cosmetic ingredient over the world.


Pharmaceutical ingredient ‘DW – EGF’

↓

Cosmetic ingredient ‘sh-oligopeptide-1’
4. DW-EGF in Easydew: High activity and safety

- Compared to other EGF, DW-EGF has higher activity according to test result.

**Highest Biological Efficiency**

![Graphs showing receptor binding activity and mitogenic activity](image)

- Measure up to the standard of Microbial contamination, Febrile substance, allergen etc.

<table>
<thead>
<tr>
<th>Item</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterility</td>
<td>No bacterial growth</td>
</tr>
<tr>
<td>Endotoxin</td>
<td>&lt;10 EU/mg</td>
</tr>
<tr>
<td>Total DNA</td>
<td>&lt;10 ppm</td>
</tr>
<tr>
<td>Host cell protein</td>
<td>&lt;100 ppm</td>
</tr>
</tbody>
</table>

**Safety Test**

<table>
<thead>
<tr>
<th>Test item</th>
<th>Effects on CNS/ Autonomic nervous system/ CV system</th>
</tr>
</thead>
<tbody>
<tr>
<td>General/Safety pharmacology</td>
<td></td>
</tr>
<tr>
<td>Toxicity</td>
<td>Acute and multiple dose (Mice, Rat, Monkey)</td>
</tr>
<tr>
<td></td>
<td>- Oral, topical, SC, IV</td>
</tr>
<tr>
<td></td>
<td>Genetic toxicity</td>
</tr>
<tr>
<td></td>
<td>Reproductive toxicity</td>
</tr>
<tr>
<td></td>
<td>Immunotoxicity</td>
</tr>
<tr>
<td></td>
<td>Other toxicity</td>
</tr>
<tr>
<td></td>
<td>Eye irradiation, skin irradiation</td>
</tr>
</tbody>
</table>

**Animal Test**

- Source: Relative potency (%)
  - Daewoong: 100
  - Roche: 85
  - NIBSC standard: 43
  - R&D Systems: 18
  - Sigma: 2

**Pharmacokinetics**

- ADME

**Clinical Trial**

- Diabetic foot ulcer (P1, P2, P3)
- Oral mucositis (P2, P3)
- Acute skin wound (P2, P3)
- Corneal wound (P1)
4. DW-EGF in Easydew What makes it different?

- 34 patents in 23 countries including America, Canada, China, Russia etc.

‘DW-EGF’ -- recognized by the whole world
4. DW-EGF in Easydew What makes it different?

# DW-EGF in cosmetics is biocompatible to the skin and can be absorbed easily by taking advantage of Liposome Technology.

‘DW-EGF’ is made as an ingredient that suits the skin best
Daewoong Pharmaceutical is the only EGF Cosmetic Quality Inspection Agency that has been authorized by KFDA. It’s available to get accurate testing results on the EGF confirmation, purity, amount etc.

The safe ‘DW-EGF’ made by Daewoong Pharmaceutical with credibility
Applications of DW-EGF in Cosmetics

- pharmaceutical grade ingredient
- treatment after hair transplantation
- skin barrier protection
- wrinkle/dermains improvement
- dermatitis after radiation exposure

DW-EGF is a pharmaceutical grade ingredient and its structure has a similarity of 99.5% with the EGF in human body.

EGF is highly effective on wound healing that can help to cure numerous fine wounds during hair transplantation.

(The clinical test results of DW-EGF product(10ppm contained) during 4 weeks conducted by Dermapro Agency)
Clinical Efficacy of DW-EGF

Cell Activation Effect

KI-67 positive cells in the skin of pig increased after testing EGF.

Collagen and Fibronectin Synthesis Promoting Effect

Compared to the control group, fibroblasts with EGF 10ng/ml increased 2 times, collagen synthesis increased by 40% and fibronectin synthesis increased by 210%.
Clinical Efficacy of DW-EGF

Cell Migration and Proliferation Effect

Scar Prevention Effect

Effect on Human Skin Fibroblast-Populated Collagen Gel Contraction: Possible Inhibitory Effect of DWP401 (rhEGF) on Scar Formation

Antagonistic Action of DWP401 (rhEGF) on TGF-β1-Induced Collagen Contraction: Possible Inhibitory Effect of DWP401 (rhEGF) on Scar Formation
Clinical Efficacy of DW-EGF

Mucositis Prevention Effect

Inflammation Inhibition Effect

Reaction rate according to RTOG grade after 4-5 weeks' radiation treatment

Inflammatory cells decreased remarkably after EGF treatment

EGF-treated group: 32.6±8.8 cells
Control group: 52.4±16.2 cells

Clinical Efficacy of DW-EGF

Hair loss-prevention Effect & Hair Restoring Effect

- Anticancer hair loss model

- Mouse hair removal model

Burn-healing Effect

Silver sulfadiazine (Ag-SD) is a useful antibacterial agent for wound treatment

- Recent findings: Ag-SD delays the wound-healing process

Comparing keratinocytes treated with different amounts of EGF and Ag-SD, there was a dose-dependent phenomenon and cyto-protective effect

The contrast of wound closure 7 days after partial thickness burn mouse model

EGF can control the delay of wound healing due to Ag-SD