What’s next in anti-ageing treatment

In-cosmetics Milan 29th March 2011
What’s next in anti-ageing?

Some ingredients (by INCI NAME)

- Acetyl Hexapeptide-8
- Acetyl Hexapeptide-30
- Tripeptide-10
- Pentapeptide-18
- Hexapeptide-10
- Palmitoyl Oligopeptide
- Palmitoyl Pentapeptide-4
- Palmitoyl Tetrapeptide-7
- Acetyl Octapeptide-3
What’s next in anti-ageing?

Examples from CTFA dictionary

INCI name: Tripeptide-10
is a synthetic peptide containing lysine, threonine, phenylalanine

INCI name: Acetyl Hexapeptide-8
is the reaction product by acetic acid and Hexapeptide-8
What’s next in anti-ageing?

Examples from CTFA dictionary

**INCI name: Tetrapeptide-7**
is a synthetic peptide containing arginine, glutamine, glycine, proline

**INCI name: Palmitoyl Tetrapeptide-7**
is the reaction product by palmitic acid and Tetrapeptide-7
What’s next in anti-ageing?

ATP 23

Azeloyl Tetrapeptide-23
ATP 23

is the reaction product by azelaic acid and Tetrapeptide-23

Tetrapeptide -23
is a synthetic peptide containing 2 moles of
Alanine and Histidine
Azelaic acid delivers 2 dipeptides (ALA-HIS)

\[ \text{ALA-HIS- azeloyl- ALA-HIS} \]

taking to Tetrapeptide.
The structure

The lipophilic chain of the dicarboxylic acid is medium (C9) and rigid (saturated) with two hydrophilic molecules at the opposite, having a strong ionic activity.
ATP 23

Azelaic Acid

L- Alanine  L- Histidine

L- Alanine  L- Histidine
What’s next in anti-ageing?

Some examples of efficacy tests as **Antiwrinkle - Antiage**

- Inhibition of the release of glutamate on neurons
- Fibrillogenesis modulation
- Reduces clusters AChR
- Inhibition of Catecolamine release (SNARE complex)
- Stimulation of GCP2 expression
- Increase collagen and GAG synthesis
- Increase skin flexibility and profilometry on volunteers
What’s next in anti-ageing?

ATP 23
Azeloyl Tetrapeptide-23

Anti-glycation active ingredient

Anti-oxidant active ingredient
What’s next in anti-ageing?

Ageing is a process involving slow deterioration in tissue function and occurs in most organs in the body, including the skin (intrinsic ageing). Recently, other factors such as glycation and AGEs (Advanced Glycation End product) formation have been involved.

**Glycation** (aka non-enzymatic glycation) is the result of the bonding of a protein or lipid molecule with a sugar molecule, such as fructose or glucose, without the controlling action of an enzyme.
What’s next in antiaging?

Stable adducts are obtained on proteins, known as
Advanced Glycation End products or AGEs.

AGEs accumulation induces:
- The loss of bioenergetic capacity in ageing skin.
- Increased senescence in keratinocytes
- Collagen glycation triggers the formation of aged skin
- Increased stiffness and lost of elasticity
- Damaged matrix proteins, reduced solubilization and decreased proteolytic activity and repair
ATP 23 acts as a sort of antagonist in the formation of links between residual amino acids of the collagen chains (lysine) with sugars. It blocks ionic exchanges between amino acids and proteinic chains. Skin ageing is in fact affected by the formation of agglomerates of glycated proteins, that becomes rigid, inflexible and aged.

The presence of dicarboxylic medium chain acid is useful to “bridge” collagen increasing its motility and elasticity. Effect is to slow down skin ageing signs.

Anti glycation activity of ATP 23 has been evaluated, in order to determine prevention of the formation of glycosylated proteins, in particular on collagen.
ATP 23

Anti glycation *in vitro* activity

*In vitro* tests on keratynocytes confirm that ATP 23 is able to inhibit AGEs (Advanced Glycation End product) formation on human fibroblasts up to 50%
Human skin is also affected by the superimposed additional changes or ‘accelerated ageing’ that result from environmental damage. This latter process is mainly due to UV irradiation from the sun and is termed Photoageing.

This process is mediated by the formation of ROS (reactive oxygen species) and free radicals.
Structures targeted by ROS

- LIPIDS
  - Damage to cell membranes

- DNA
  - Mutations
  - Toxic product formation

- PROTEINS
  - Sulphidrile-dependent enzymes disturbances

- COENZIMES
ATP 23 thanks to its peculiar structure prevents skin lipids peroxidation, protecting cellular membrane from scavengers attacks.

ATP 23 blocks free radicals and skin ageing
ATP 23

Anti-oxidant *in vitro* activity

*In vitro* test confirms that ATP 23 shows antioxidant activity inhibiting lipids peroxidation over 60%
ATP 23

*in vitro* Scavenging activity

*In vitro* test confirms that ATP 23 reduces 40% Reactive Oxygen Species (ROS) production in human keratynocites after UVA irradiation.

![Reduction of UVA-induced ROS on keratynocites](chart.png)

<table>
<thead>
<tr>
<th>Concentration (%)</th>
<th>4 min UVA</th>
<th>8 min UVA</th>
<th>12 min UVA</th>
<th>16 min UVA</th>
<th>20 min UVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>50.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>25.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>12.50</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>6.25</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>3.12</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>1.56</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>0.78</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>0.39</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>0.19</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>
ATP 23

**in vitro** Scavenging activity

*In vitro* test confirms that ATP 23 reduces 45% Reactive Oxygen Species (ROS) production in human keratynocites if not UVA irradiated.
ATP 23

*in vitro* scavenging activity

ATP 23 demonstrated a free radical scavenging capacity

- helping aged skin from environmental free radicals
- preventing skin ageing from endogenous free radicals
ATP 23

Anti-age in vivo efficacy test*

PROTOCOL

• 12 volunteers, twice a day for 6 weeks
• Area of application: face
• Product: ATP 23 emulsion 5% versus placebo
• Clinical evaluation: ANTI AGE - ANTI WRINKLE EFFECT
• Instrumental evaluation: elasticity, hydration, skin density, brightness
• Instrumental evaluation: Skin roughness, smoothness profilometry (Primos)
• Skin and eyes tolerability and Self assessment
### ATP 23

#### Anti-age in vivo efficacy test

**Elasticity (R0)**

<table>
<thead>
<tr>
<th></th>
<th>$T_0$</th>
<th>$T_{3 \text{ WEEK}}$</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLACEBO</strong></td>
<td>Mean 0.248, std.dev. 0.068</td>
<td>Mean 0.249, std.dev. 0.045</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>ATP 5% CREAM</strong></td>
<td>Mean 0.258, std.dev. 0.063</td>
<td>Mean 0.229, Std.dev. 0.069</td>
<td>-11.2%</td>
</tr>
</tbody>
</table>

*conclusive results at 6 weeks are in progress*
## ATP 23

### Anti-age in vivo efficacy test *

Mean Roughness (Sa)

<table>
<thead>
<tr>
<th></th>
<th>$T_0$</th>
<th>$T_{3\text{sett.}}$</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLACEBO</strong></td>
<td>Mean 63.58, Std. dev. 21.31</td>
<td>Mean 64.67, Std. dev. 22.48</td>
<td>1.7%</td>
</tr>
<tr>
<td><strong>ATP 5% CREAM</strong></td>
<td>Mean 59.50, Std. dev. 22.70</td>
<td>Mean 53.92, Std. dev. 16.45</td>
<td>-9.4%</td>
</tr>
</tbody>
</table>

* conclusive results at 6 weeks are in progress
ATP 23

Anti-age in vivo efficacy test

3D Photo image by Primos

before treatment

After 3 weeks
ATP 23

Anti-age in vivo efficacy test

3D Photo image by Primos - HIGH DEFINITION

before treatment

After 3 weeks
# ATP 23

## Anti-age *in vivo* efficacy test *

### Skin density

<table>
<thead>
<tr>
<th></th>
<th>$T_0$</th>
<th>T $3$ WEEKS</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLACEBO</strong></td>
<td>Mean 26.01</td>
<td>Mean 25.53</td>
<td>-1.8%</td>
</tr>
<tr>
<td></td>
<td>std. dev 4.51</td>
<td>std. dev 4.86</td>
<td></td>
</tr>
<tr>
<td><strong>ATP 5% CREAM</strong></td>
<td>Mean 25.55</td>
<td>Mean 27.03</td>
<td>+5.8%</td>
</tr>
<tr>
<td></td>
<td>std. dev 3.80</td>
<td>Std. dev 4.28</td>
<td></td>
</tr>
</tbody>
</table>

* conclusive results at 6 weeks are in progress
Anti-age in vivo efficacy test

Ultrasound high definition image by Dermascan

before treatment

After 3 weeks
ATP 23

Anti-age *in vivo* efficacy test*

RESULTS

- Photo imaging analysis (by Primos instrument) has evidenced a clinical reduction *(already 10% at 3 weeks)* of profilometric parameters. Wrinkles appear less evident and deep.

- ATP 23 showed also an activity as enhancer of skin elasticity, density and brightness

* conclusive results at 6 weeks are in progress
Conclusions

ATP 23 is indicated for the treatment of skin ageing:

- prevents expression wrinkles.
- regenerates the skin barrier with high level cosmetic effects
- slows down trends of skin ageing features (wrinkles, dryness, dullness, laxity).

a second generation active ingredient
ATP 23

CAS NUMBER 1263306-88-2

INCI NAME (suggested) Azeloyl Tetrapeptide-23
ATP 23

Toxicological profile

Primary skin irritation test \textit{(in vivo)}: NOT irritant
(patch test 10\% sol.)

Primary skin irritation test (human reconstituted epidermis) (ECVAM – ESAM validated protocol): NOT irritant

Ocular irritation test (human corneal reconstituted epidermis)
MTT citotoxicity: NOT irritant

Skin sensitisation \textit{(in vitro)}: NOT sensitising
ATP 23

TECHNICAL SPECIFICATIONS

Appearance: Clear liquid
Color: white to pale yellow
Odour: neutral, characteristic
Dry residual: 23 -28%
pH: 5.0-7.0
Active content: 4-6%

Preservation system:
Potassium sorbate: 0.1-0.3%
Sodium benzoate: 0.3- 0.5%
Sodium dehydroacetate: 0.1-0.3%
COSMETIC APPLICATIONS

ATP 23

Advanced pro-age peptide that inhibits the glycation of dermal proteins and slows down the oxidative damage. Recommended for aged skin, preventing expression wrinkles and renews skin cells.
## ATP 23 Compatibility

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citric Acid, Lactic Acid</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Sodium Hydroxide, Aminomethyl Propanol</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Glycerin</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Sorbitol</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Xylitol</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Propylene Glycol</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Butylene Glycol</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Alcohol denat.</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
### Compatibility with Rheological Additives

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyethylcellulose</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Hydroxypropyl Guar</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Carbomer</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Acrylates/C10-30 Acrylate Crosspolymer</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Sodium Acrylates</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Xanthan Gum</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Sclerotium Gum</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Cellulose Gum</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Polyacrylamide</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Chondrus Crispus(Carrageenan)</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
### ATP 23

**Formulary guide**

**Pro Age Advanced Serum**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>% w/w</th>
</tr>
</thead>
<tbody>
<tr>
<td>HITECREAM 3000 (SINERGA)</td>
<td>3.00</td>
</tr>
<tr>
<td>TRISOLVE (SINERGA)</td>
<td>2.00</td>
</tr>
<tr>
<td>Cyclopentasiloxane and Dimethicone/Vinyl Dimethicone Crosspolymer</td>
<td>15.00</td>
</tr>
<tr>
<td>TREALIX (SINERGA)</td>
<td>2.00</td>
</tr>
<tr>
<td>Parfum</td>
<td>0.50</td>
</tr>
<tr>
<td>Aqua</td>
<td>to 100</td>
</tr>
<tr>
<td>Cyclomethicone</td>
<td>5.00</td>
</tr>
<tr>
<td>Disodium Edta</td>
<td>0.10</td>
</tr>
<tr>
<td>FENICAP (SINERGA)</td>
<td>1.0</td>
</tr>
<tr>
<td>Glycerin</td>
<td>3.00</td>
</tr>
<tr>
<td>ATP 23 (SINERGA)</td>
<td>5.00</td>
</tr>
<tr>
<td>Sodium polyacrylate</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Sinerga Commercial Department*
ATP 23

Formulary guide

Antiage cream

Rejuvenating nourishing cream

Timeless Cream

and more.......
Acknowledges and thanks for support to

- **ABICH** laboratories for *in vitro* tests
  (www.abich.it)

- **ISPE** laboratories for clinical evaluations
  (www.ispe.it)

- **SINERGA** Research center
  (www.sinerga.it)
THANKS

Visit

STAND Q70
IN FOCUS area
IN-COSMETICS MILANO
29-31 march 2011

contact:
g.guglielmini@sinerga.it