Introduction

In the conventional administration method, only applying active ingredients of cosmetics to skin, it was difficult for the ingredients to penetrate deep in skin and to fully exert their beautifying effect and skin protection effect. That is because the HLB (Hydrophile-Lipophile Balance) values of the ingredients are improper and active ingredients are unstable and subject to oxidative decomposition.

Then, iontophoresis that is a method to penetrate an ionized solvent into skin deeply by passing feeble current through skin has been emerging as a new skin care method from several years ago. Unfortunately, most of existing iontophoresis treatment devices are nominal “iontophoresis”. They have no clinical records and physical grounds. Most of them lack safety and stability, and have just low level of penetration (total vitamin C).

VITALIONT II was developed five years ago in cooperation with Dr. Harue Suzuki, the director of Suzuki Plastic Surgery Clinic in Kyoto as of now. The permeability of total vitamin C by use of VITALIONT II was demonstrated by a research group under the leadership of Prof. Nobuhiko Miwa in School of Bioresources of Hiroshima Prefectural University, and its clinical records have been favorable. Key points in iontophoresis are penetration rate, stability, and durability. We, Indiba-Japan Co., Ltd. have pursued the study of iontophoresis to make improvements functionally and effectively.

The correlation between electric characteristics such as supportability of hardware and software i.e. waveform/duty ratio, material and shape of the electrode, etc. and applying solvent is also an important subject. In consideration of important points like the above, the first prototype was completed in January, 2002 after modifications and improvements one after another. We asked Dr. Suzuki and Prof. Miwa to have final clinical tests and final experiments immediately after the device completion. As the results of the tests and experiments, it became obvious that penetration rate, stability, durability, supportability of hardware and software, and other factors are all highly satisfactory, then the world's first iontophoresis treatment device equipped with newly developed functions, “HIGH VITALIONT”, has finally emerged.
**Research Results (regarding "HIGH VITALIONT") (H.V., named tentatively)**

(1) Most excellent iontophoresis to both epidermis and dermis was accomplished, and total vitamin C penetration rate and stability has been significantly increased at the maximum current value of 1.0 mA without feeling tingled. (See experiments 1, 2, and 3 in Fig. 1. Pay attention to the values.)

Note: For face and neck, 1.0 mA is selected.

(2) The concentration of vitamin C stays between 2240 µM and 3890 µM at epidermis, which is approximately 1000 times thicker than existing devices (including competitors' products), and the level of vitamin C in the blood is 56 - 97 times thicker. This value even at dermis stays between 127 µM and 281 µM, which is over 200 times thicker than existing devices (including competitors' products). (See experiments 1, 2, and 3 in Fig. 1.) It is demonstrated that the permeability of vitamin C by HIGH VITALIONT has been substantially increased comparing with conventional types because vitamin C can be hardly found in dermis after applying solvent to skin.

**Fig. 1 Total amount of vitamin C**

<table>
<thead>
<tr>
<th>Experiment 1</th>
<th>Experiment 2</th>
<th>Experiment 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>4% Asc2P-Na</td>
<td>4% Asc2P-Na</td>
<td>4% Asc2P-Na</td>
</tr>
</tbody>
</table>

- **Epidermis**: H.V.
- **Dermis**: Company B
- **Application**: Company T

<table>
<thead>
<tr>
<th>Skin to be tested</th>
<th>Flank (17-year-old female)</th>
<th>Upper eyelid (33-year-old female)</th>
<th>Groin (21-year-old female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin thickness</td>
<td>0.098mm 2.2mm</td>
<td>0.072mm 0.9mm 1.23mm</td>
<td>0.094mm 1.23mm</td>
</tr>
<tr>
<td>Iontophoresis</td>
<td>8min</td>
<td>8min</td>
<td>8min</td>
</tr>
<tr>
<td>Cultivating time after iontophoresis</td>
<td>4hr.</td>
<td>4hr.</td>
<td>4hr.</td>
</tr>
</tbody>
</table>

Displayed actual current value
- H.V. (0.3mA)  Company B (0.3mA)  Company T (0.3mA)  Application (–)

Actual current value in body
- (0.02mA)  (0.02mA)  (0.02mA)  (–)

- H.V. (0.65mA)  (0.06mA)  (0.10mA)
The reduction rates of vitamin C with HIGH VITALIONT stay between 97% and 100%. On the other hand, the reduction rates with other companies' iontophoresis devices stay between 30% and 60%. The reduction rate of vitamin C is an index that indicates how much vitamin C converted from provitamin C is maintained in the form of reductive vitamin C that is stable in the pharmacologic effect.

The following conversion is executed in skin.

Provitamin C -> Vitamin C (ascorbic acid) -> Dehydro ascorbic acid -> Decomposition

The reduction rate is an index that indicates the percentage of ascorbic acid in the total vitamin C, which means the resistance to oxidative decomposition or stability (vitamin C stabilization rate). (See Fig. II.)

(Applying solvent) Indiba-Japan Co., Ltd. is now working toward developing new provitamin C, A, E, etc. with our sights set on improving the iontophoresis effect.

Fig. II Vitamin C stabilization rate (%)
Effectiveness

New iontophoresis treatment device (HIGH VITALIONT) and provitamin C penetration

The high effectiveness of iontophoresis in treatment is demonstrated due to the establishment of new functions.

A) Sufficient amount of vitamin C should be supplied to the basal layer of epidermis to suppress abnormal increase in melanin that causes pigmentation such as chloasma, freckle, and transient pigmentation (after laser irradiation) and to decolorize already-existing melanin.

B) Wrinkle

It is required to hydrate proline/lycine residue in alpha-chains to form triple helix by the polymerization of 3 pieces of preprocollagen alpha-chains regarding dermis fibroblast. It is significant to supply vitamin C intentionally as an essential cofactor to make propyl-4-hydroxylase function as a main enzyme to catalyze the reaction above because vitamin C is apt to be depleted partially.

C) Elimination of active oxygen

The elimination of active oxygen by intracellular vitamin C can prevent deep-penetrating UVA-wave from causing nuclear DNA double-strand breaks and damage to DNA base components such as 8-OHdG.

D) Prevention of skin aging

Provitamin C can be, in the DNA level, an age resistor that significantly extends cell life by preventing telomere DNA located at both ends of chromosomes from shortening.

E) Hyperoxidation of sebum such as squalene and ceramide has a deleterious effect on skin. Provitamin C prevents cell death caused by lipoperoxide.

Addendum (1): Our new device can remove pore-clogging grime after washing your face by use of negative-polarity before iontophoresis. At that time, purified water can be used but skin toner manufactured by Natura Bisse is more effective.

Addendum (2): We have 3.75 and 7.5 % of provitamin C, 50 % of placenta liquid, 7 % of bearberry extract, etc. for an applying solvent. We are also studying the possibility of more effective solvents including other application purposes.

Medical & technical advisors:

1) Harue Suzuki, M.D. of Suzuki Plastic Surgery Clinic, Kyoto
2) Nobuhiko Miwa, Prof. of School of Bioresources at Hiroshima Prefectural University

Specifications

1) Attaché case type (aluminum color)
2) Timer: Maximum 15 minutes, output up/down adjustment, beep after set time lapse
3) Polarity +/- button: negative when setting to ON, beep
4) Two-stage power adjustment: Low 0 mA-1.2 mA
   High 1.3 mA-2.4 mA
   beep at switching
5) Output can be locked after power adjustment. Stable iontophoresis available
6) Note: The efficacy of iontophoresis is substantially enhanced comparing with conventional type thanks to modification of waveform, increase in frequency, and other improvements.