Feasibility of Atmospheric Argon Plasma for Improving Transdermal Drug Absorption

Nhat An Tran[1], Jaroslav Kristof[2], Marius Gabriel Blajan[3] and Kazuo Shimizu[1,2,3]

[1]Graduate School of Engineering Shizuoka University [2] Graduate School of Science and Technology, Shizuoka University

[3]Organization for Innovation and Social Collaboration, Shizuoka University

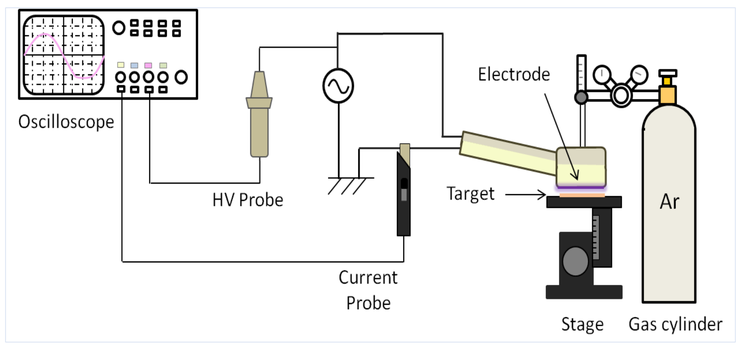
1. Introduction

Drug delivery through the skin has been recognized as an important route. However, the transdermal route is still limited to delivery of small, lipophilic and low-dose drugs. We investigated the effect of atmospheric pressure argon nonthermal plasma irradiation on reducing skin barrier function as a promising solution.

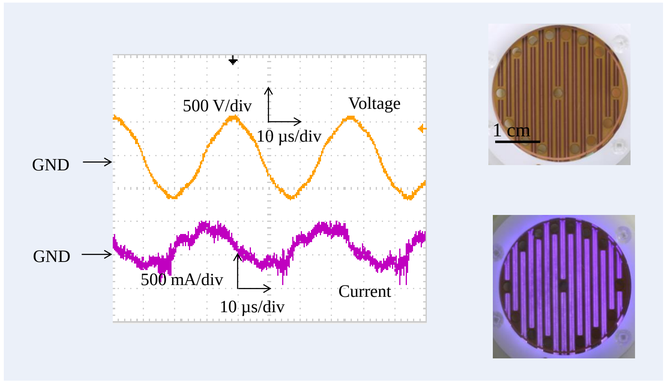
Atmospheric pressure nonthermal plasmas has been demonstrated to be appropriate for skin treatment such as wound healing, tissue regeneration or wrinkle treatment. In this study, a promotion of transdermal drug absorption by the atmospheric argon plasma irradiation was investigated. The results were analyzed by using an infrared total reflection absorption measurement (ATR) method and transepidermal water loss (TEWL) measurement.

2. Experiment Setup and Method

Microplasma



- **Target: Yucatan micropig skin**
- Power Source: 27.1 kHz AC
- Applied Voltage: 700 V (0-P)
- Process Gas: Argon
- Exposure time: 1 min, 5 min
- Exposure distance: 7 mm



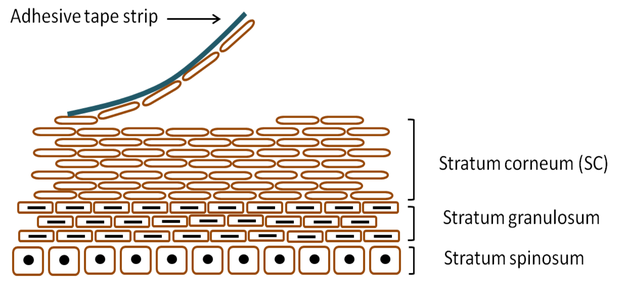
Advantages of Microplasma

✓ No need of costly vacuum enclosures

✓ Including highly reactive species, charged species

✓ Simple equipment structure

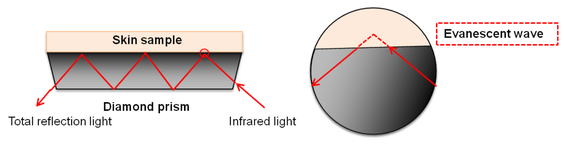
Tape Stripping



- Target: Yucatan micropig skin
- Tape: Scotch Tape
- Number of tape stripping: 10, 20 cycles
- Pressure on the skin: 165 g/cm^2

Stratum corneum (SC) layers were physically removed → Barrier function of the SC was certainly reduced

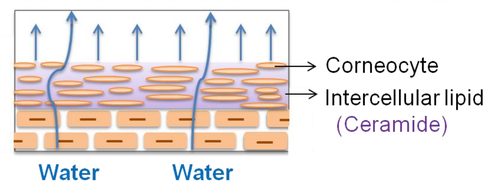
ATR Method



- Prism: Diamond
- Resolution: 4.0 cm^{-1}
- Cumulated number: 64 times

TEWL Measurement

Amount of released water = TEWL



Increased TEWL → Reduced barrier function

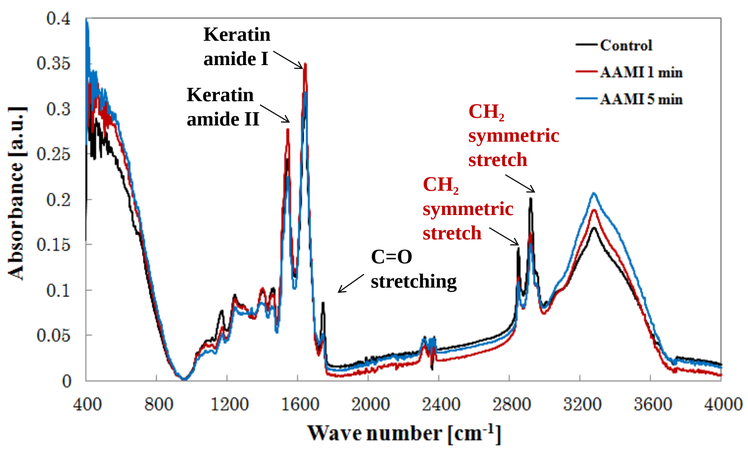
3. Results

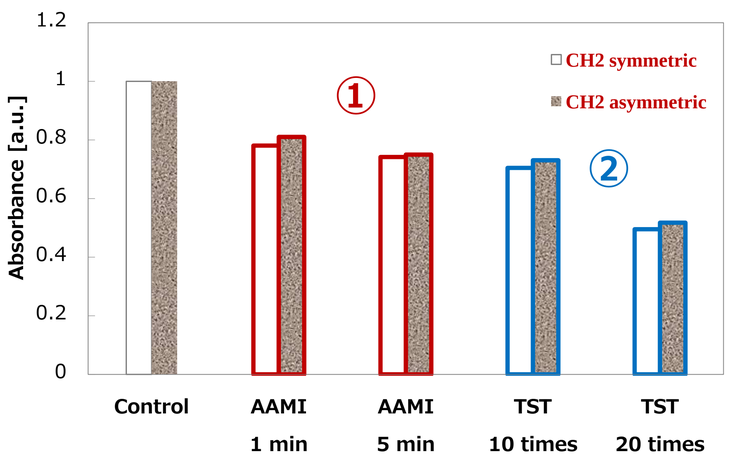
ATR-FTIR Analysis

FTIR = Fourier Transform Infrared Spectrometer

AAMI = Atmospheric Argon Microplasma Irradiation

TST = Tape Stripping Test



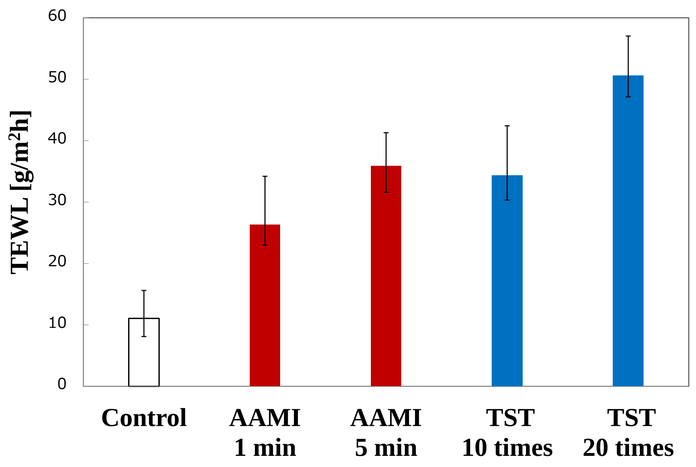


① Increase in plasma exposure time → **Reduction in the CH_2 stretching modes absorbance**

② Increase in the number of tape strips → **Reduction in the CH_2 stretching modes absorbance**

Disturbance in the SC lipids

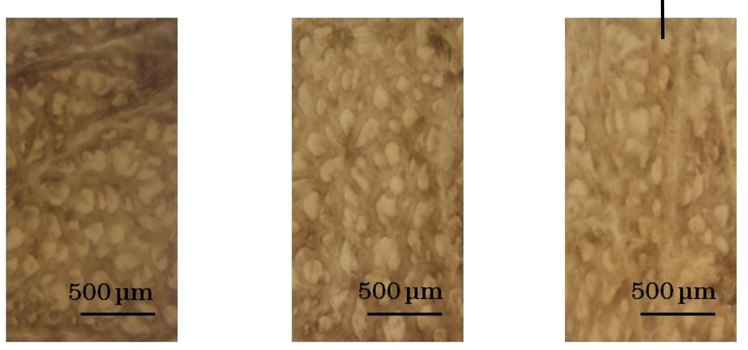
TEWL Measurement



Increase in plasma exposure time → Increase in TEWL value → **Barrier properties of the skin were decreased**

Microscopic observation

Decrease in asperity of stratum corneum layer



(a) Control (b) AAMI 5 min (c) TST 20 times

Microplasma irradiation → Damage on the skin

4. Conclusions

- **The reduction in the CH2 stretching peaks reflects the disturbance in the SC lipids after AAMI.**
- **TEWL value was decrease for both of AAMI and TST, which suggests that the barrier function of the SC was decreased.**
- **The microscopic observation indicated that AAMI does not lead to physical damages on a skin.**

→ **Alternative technology for normal injection needles**