Transdermal Drug Delivery Using Microplasma

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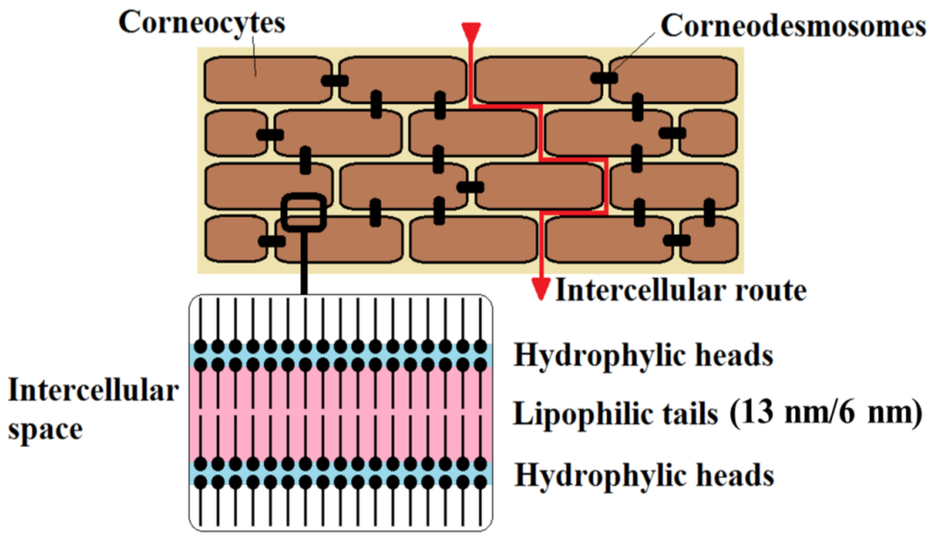
Introduction. **Stratum corneum is first barrier that protect our body and does not allow penetration of amount of objects such as drugs. Intercellular route is very often used for drug penetration when stratum corneum lipids are extracted or their structure is changed. This study investigate transdermal delivry of Cyclosporine A using Micrplasma treatment.**

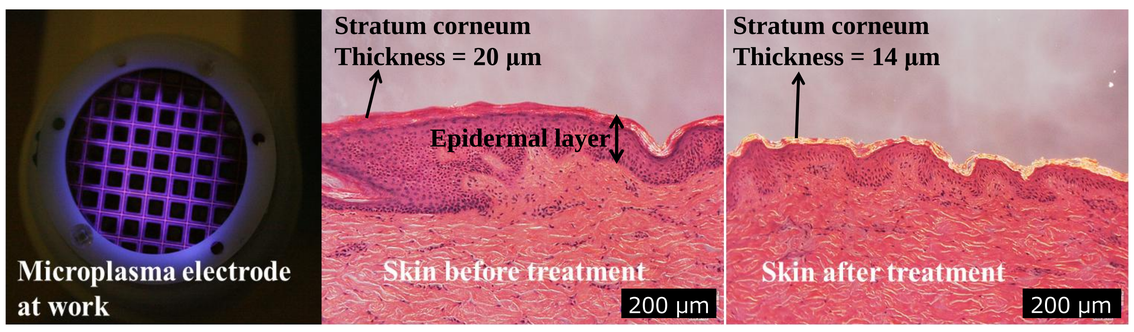


Influence on penetration of drug

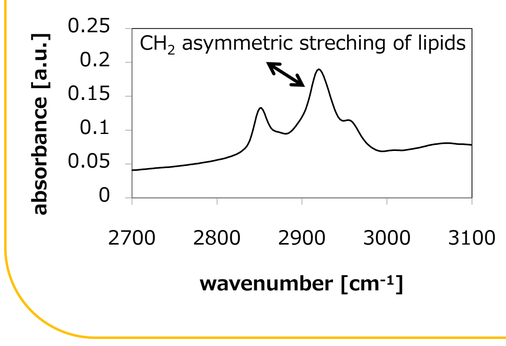
Intercellular space
- Structure
- Composition

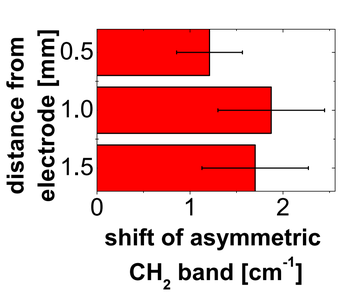
Stratum corneum
- Thickness

Etching effect of microplasma



Structure change of lipids of the stratum corneum



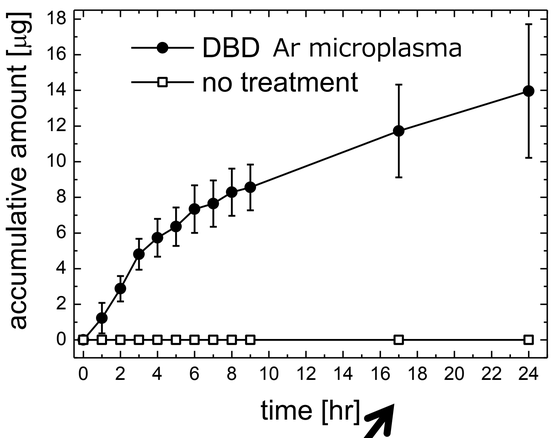


Shift to higher wavenumbers

Higher permeability

Cyclosporine A penetration

Ar microplasma treatment increased skin permeability to allow Cyclosporine A penetration



No penetration was observed in the case of

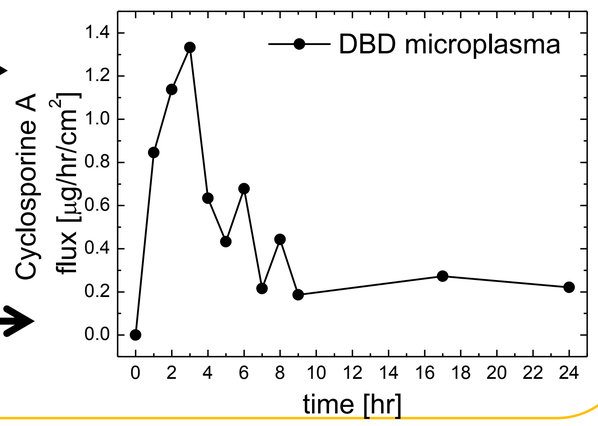
→ "no microplasma treatment"

→ air microplasma treatment

→ $Ar+H_2O_2$ plasma treatment (or low amount of drug)

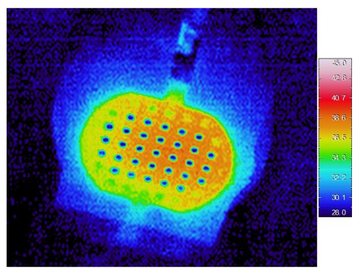
After 24 hours, 14 µg of Cyclosporine A was penetrated trough the skin

Maximum penetration rate of drug is reached after 3 hours

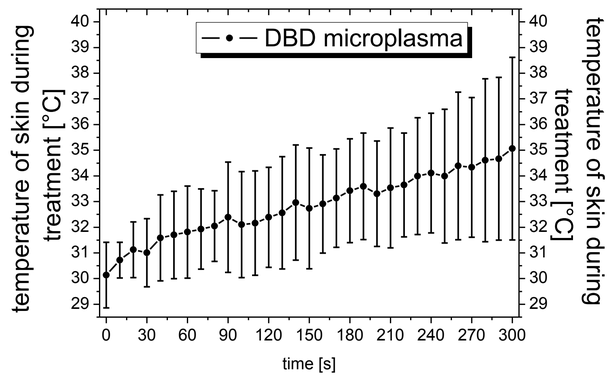


Temperature safety

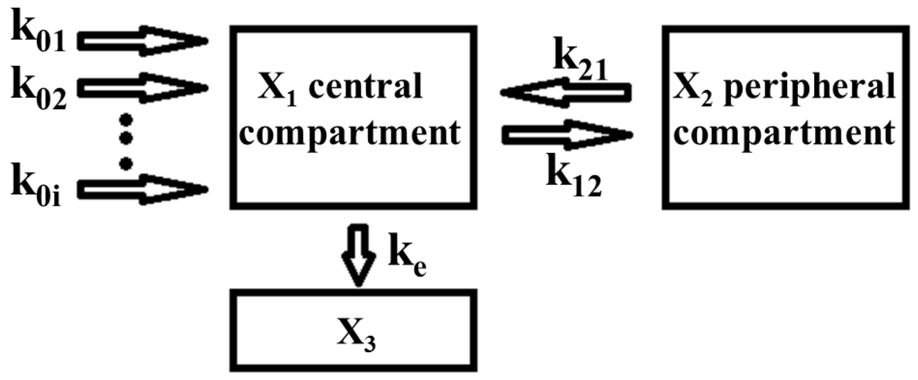
Ar microplasma discharge



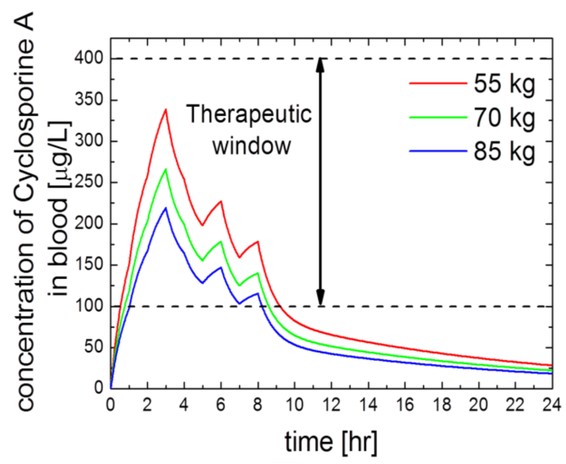
Skin temperature is under 45°C – No temperature damage of the skin



Pharmacokinetics

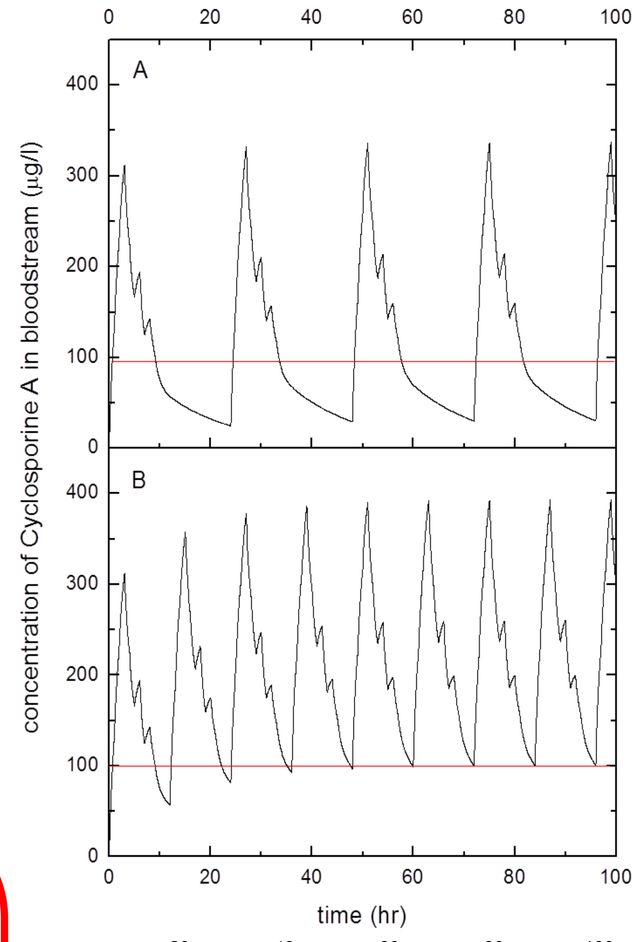


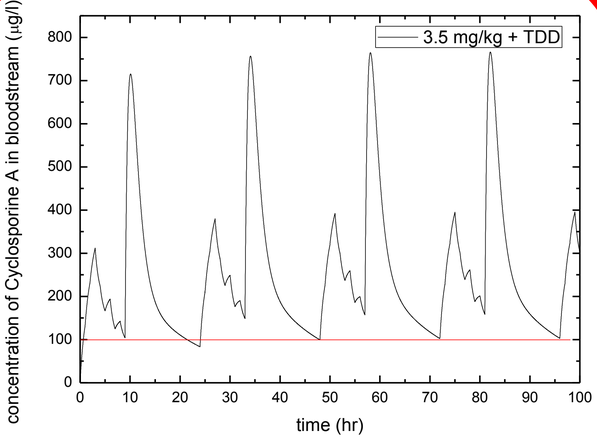
central compartment X_1 represents blood. Cyclosporine A is delivered to blood with flux k_{0i} (in µg/hr) and it is eliminated from the body at rate constant k_e. The second, peripheral compartment X_2 consists of tissues, bones, skin, etc. Drug exchange between the central and peripheral compartments is controlled by rate constants k_{12} and k_{21}.



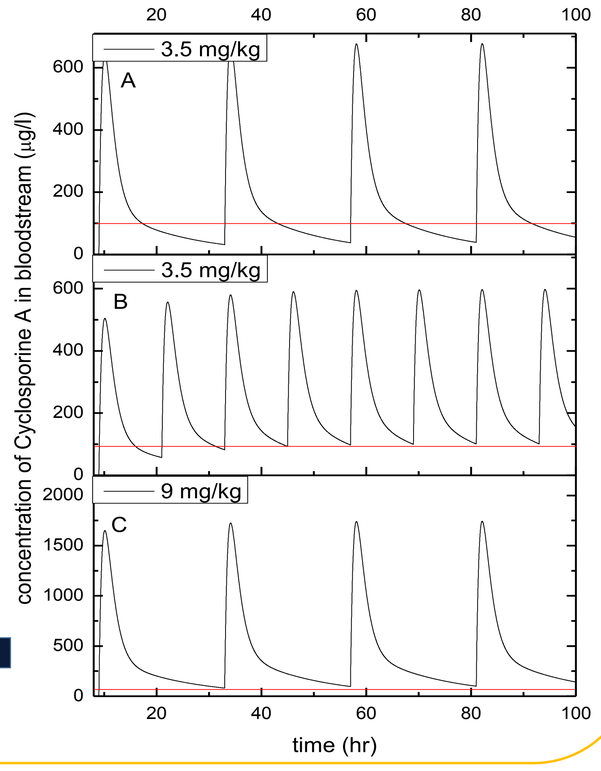
400 mg/ml of Cyclosporine A was applied to 225 cm² (15x15 cm) (model)

Repeated microplasma treatment
A) Every 24 hours
B) Every 12 hours





Combination of oral delivery with transdermal delivery



Repeated oral delivery
A) Every 24 hours (3.5 mg/kg)
B) Every 12 hours (3.5 mg/kg)
C) Every 24 hours (9 mg/kg)

Conclusions

- Applying of Ar microplasma increases permeability of the skin
- Air microplasma does not increase skin permeability and gaseous H_2O_2 in mixture with Ar decrease (no penetration)
- Skin treatment is safe and no heat or electrical damege can happen
- It is possible to achieve therapeutic concentration of Cyclosporine A in the blood if 400 mg/ml of Cyclosporine A in propylene glycol is applied
- Microplasma drug delivery can decrease amount of the drug administered orally and to decrease interactions in gastrointestinal tract