Transdermal delivery of biologics using microneedles and other technologies

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Outline of Talk

Three generations of transdermal delivery
- no enhancement needed
- increase stratum corneum permeability
- increase permeability targeted to stratum corneum

Delivery of biologics using microneedle patches
- human studies of microneedle patches
- influenza vaccination
Transdermal drugs approved by the US FDA

Histological structure of human skin

stratum corneum
viable epidermis
dermis
Three generations of transdermal delivery

1\textsuperscript{st} generation
· conventional patches

2\textsuperscript{nd} generation
· chemical enhancers
· non-cavitational ultrasound
· iontophoresis

3\textsuperscript{rd} generation (nano and micro)
· cavitational ultrasound
· electroporation
· chemical enhancer mixtures
· microneedles
· thermal ablation
· microdermabrasion
Three generations of transdermal delivery

1\textsuperscript{st} generation
\begin{itemize}
  \item conventional patches
\end{itemize}

2\textsuperscript{nd} generation
\begin{itemize}
  \item chemical enhancers
  \item non-cavitational ultrasound
  \item iontophoresis
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3\textsuperscript{rd} generation (nano and micro)
\begin{itemize}
  \item cavitational ultrasound
  \item electroporation
  \item chemical enhancer mixtures
  \item microneedles
  \item thermal ablation
  \item microdermabrasion
\end{itemize}

No enhancement needed
1st generation transdermal delivery

stratum corneum
viable epidermis
dermis
1\textsuperscript{st} generation transdermal delivery

stratum corneum
viable epidermis
dermis
Three generations of transdermal delivery

1\textsuperscript{st} generation
- conventional patches

No enhancement needed
Limited to drugs with appropriate properties

2\textsuperscript{nd} generation
- chemical enhancers
- non-cavitational ultrasound
- iontophoresis

Increase stratum corneum permeability

3\textsuperscript{rd} generation (nano and micro)
- electroporation
- cavitational ultrasound
- chemical enhancer mixtures
- microneedles
- thermal ablation
- microdermabrasion
2\textsuperscript{nd} generation transdermal delivery
chemical enhancer

- stratum corneum
- viable epidermis
- dermis

chemical enhancer
2nd generation transdermal delivery
noncavitational ultrasound

stratum corneum
viable epidermis
dermis

ultrasound probe
sound waves
2\textsuperscript{nd} generation transdermal delivery

iontophoresis

electrode
electrode

stratum corneum
viable epidermis
dermis

current
### Three generations of transdermal delivery

<table>
<thead>
<tr>
<th>Generation</th>
<th>Methods</th>
<th>Benefits</th>
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<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; generation</td>
<td>conventional patches</td>
<td>No enhancement needed</td>
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<td></td>
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<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; generation</td>
<td>chemical enhancers</td>
<td>Increase stratum corneum permeability</td>
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<tr>
<td></td>
<td>non-cavitational ultrasound</td>
<td>Insufficient targeting of stratum corneum</td>
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<tr>
<td></td>
<td>iontophoresis</td>
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<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; generation (nano and micro)</td>
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<td>Increased permeability targeted to stratum corneum</td>
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<td>microdermabrasion</td>
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3\textsuperscript{rd} generation transdermal delivery (nano) cavitation ultrasound

ultrasound probe

stratum corneum
viable epidermis
dermis

sound waves

Cavitational bubble activity at skin surface
3rd generation transdermal delivery (nano) electroporation

stratum corneum
viable epidermis

dermis

stratum corneum
viable epidermis and dermis

electrode
electrode

voltage
3rd generation transdermal delivery (nano) chemical enhancer mixtures

- **stratum corneum**
- Viable epidermis
- Dermis

Chemical enhancer mixture

Mixture composition dilutes and changes
3rd generation transdermal delivery (micro) microneedles

- stratum corneum
- viable epidermis
- dermis
- microneedle patch
3rd generation transdermal delivery (micro) microneedles
3rd generation transdermal delivery (micro) thermal ablation

- stratum corneum
- viable epidermis
- dermis
3rd generation transdermal delivery (micro) thermal ablation

- stratum corneum
- viable epidermis
- dermis
3\textsuperscript{rd} generation transdermal delivery (micro)

cmicrodermabrasion

\textit{stratum corneum}

\textit{viable epidermis}

dermis

\textit{microdermabrasion handpiece}
3rd generation transdermal delivery (micro) microdermabrasion
### Three generations of transdermal delivery

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- **1st generation**: No enhancement needed. Limited to drugs with appropriate properties.
- **2nd generation**: Increase stratum corneum permeability. Insufficient targeting of stratum corneum.
- **3rd generation**: Increase permeability targeted to stratum corneum. Requires devices and/or tissue removal.
Three generations of transdermal delivery

1\textsuperscript{st} generation
· conventional patches

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many successful products (no biologics)
in some patches physical therapy (NSAIDs) lidocaine, fentanyl, sweat test (no biologics)

lidocaine
research

influenza vaccine, clinical trials
clinical trials research
Outline of Talk

Three generations of transdermal delivery
- no enhancement needed
- increase stratum corneum permeability
- increase permeability targeted to stratum corneum

Delivery of biologics using microneedle patches
- human studies of microneedle patches
- influenza vaccination
Microneedles deliver drugs to the skin using a simple patch.
Microneedle research is increasing
Drug delivery mechanisms using microneedles

- Solid MN
- Coated MN
- Dissolving MN
- Hollow MN

layers:
- stratum corneum
- viable epidermis
- dermis
Microneedles deliver drugs to the skin using a simple patch.

Green dye represents location of drug.
Dissolving polymer microneedles
Dissolving polymer microneedles
Microneedles meet public health needs

**Manufacturing**
Low-cost fabrication

**Transportation and storage**
Small package size
Possible thermal stability

**Patient administration**
No reconstitution
Possible reduced dose
Minimally trained personnel

**Waste disposal**
Difficult or impossible reuse
Reduced or no disposal volume
Tolerability of placebo microneedle patch

Determine the tolerability of a placebo microneedle patch in human subjects.
Acceptability of influenza vaccination using a microneedle patch

Determine the acceptability of a placebo microneedle patch in future use for influenza vaccination in untrained human subjects.
Acceptability of influenza vaccination using a microneedle patch

- Normally vaccinated: 46%
- Normally unvaccinated: 54%
Acceptability of influenza vaccination using a microneedle patch

54% unvaccinated

- 20% IM
- 16% Normally vaccinated
- 7% HCW Applies Patch
- 3% SA w/ HCW Nearby
- 7% SA @ Home

54% vaccinated
Acceptability of influenza vaccination using a microneedle patch

- Normally vaccinated
  - 20% IM
  - 16% SA @ Home
  - 7% SA w/ HCW Nearby
- Normally unvaccinated
  - 3% HCW Applies Patch
  - 3% Other
Influenza vaccination using a microneedle patch

A phase I study of the safety, reactogenicity, acceptability and immunogenicity of inactivated influenza vaccine delivered by microneedle patch or by hypodermic needle.
Products under development

Zosano Pharma, Inc. Announces Publication of Positive Phase 2 Study of its ZP-PTH Patch for Osteo.

Radius Announces Positive Topline Data From Phase 2 Study of Abaloparatide (BA058) for Postmenopausal Osteoporosis Using Two Delivery Systems

Corium Announces Positive Topline Results From Phase 2a Study of Transdermal MicroCor(R) PTH in Post-Menopausal Women

Zosano Pharma Completes Enrollment in Phase 2 Trial for ZP-Glucagon, Its Microneedle Patch for Treatment of Severe Hypoglycemia
Summary of Talk

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Conflict of interest disclosure

Mark Prausnitz serves as a consultant and is an inventor on patents licensed to companies developing products related to this presentation. This potential conflict of interest is managed by Georgia Tech and Emory University
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Past lab members

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