Ultrasound-Enhanced Drug Delivery for Treatment of Onychomycosis

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PZFLEX

PZFLEX is an analysis software, that utilizes a finite-element approach and an explicit time-domain.

It was used to calculate the exact ultrasound intensity in both the luminosity and diffusion cell experiments at all frequencies.

It was also used to calculate temperature increase in the human toe exposed to ultrasound at DFF.

Frequency (kHz): 400 kHz, 600 kHz, 800 kHz, 1 MHz
Distance (DFF): 15.0 mm, 22.5 mm, 30.0 mm, 37.5 mm.

RESULTS

• Our data indicated that application of low-intensity ultrasound can lead to increased permeability of the nail.
• A higher frequency corresponded to more permeation through the nail.
• Temperature increases as determined by PZFLEX and thermocouples were found to be under 1.5°C, and are expected to be safe in future applications in patients.

LUMINOSITY EXPERIMENT METHODS AND MATERIALS

• Pieces of porcine nail were placed in a 100 mL beaker, 35 cm beneath the ultrasound transducer.
• The beaker filled with the blue dye which with a molecular weight of 792.84 g/mol, mimics the nail polish drugs used.
• Images were taken after treatment (Fig. 4).
• Cross section image was analyzed on Photoshop.
• Luminosity value (v) was developed using Photoshop brightness value (b).
  \( V=10b \)

DIFFUSION CELL MATERIALS AND METHODS

• The donor compartment was filled with blue dye or Ciclopirox and the receiving compartment was filled with saline or ethanol.
• The nails were placed in an adaptor between the donor and receiving compartment.
• Ultrasound was applied 8.5 cm above the nail.
• After allotted time of application of ultrasound, the nail sat with dye or Ciclopirox to total 60 min exposure.
• After 60 min exposure, the permeability of the nail was measured by the absorption of the liquid in the donor compartment.

GENERAL EXPERIMENTAL PARAMETERS

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Luminosity Intensity (W/cm²)</th>
<th>Diffusion Cell Intensity (W/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>400 kHz</td>
<td>1.02</td>
<td>.99</td>
</tr>
<tr>
<td>600 kHz</td>
<td>1.04</td>
<td>.94</td>
</tr>
<tr>
<td>800 kHz</td>
<td>1.06</td>
<td>1.03</td>
</tr>
<tr>
<td>1 MHz</td>
<td>.96</td>
<td>.99</td>
</tr>
</tbody>
</table>

Fig. 3: Intensity of luminosity and diffusion cell experiments

FUTURE STUDIES

• We plan to use mycotic human nails which are removed as part of normal treatment, in the diffusion cell setup.
• The parameters for ultrasound will be optimized within those deemed safe for humans.

CONCLUSIONS

If proven successful our method may find a clinical application due to the non-invasive nature of therapeutic ultrasound treatment. Our results show a clear correlation between the application of ultrasound at increasing frequency and permeability of the nail. This suggests that our methodology may have a place in the clinical field and the ideal parameters may be found at a higher frequency. Additionally, the temperature measurements found using PZFLEX suggest that this method is in fact safe for humans.

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