Nanoemulsion Antimicrobials Tested Against Nine Gram-Positive Species

ABSTRACT

Background: Nanoemulsions (NEs) are oil-in-water emulsions composed of pharmaceutically approved substances in nanodroplets that have an average diameter of 180 or 350 nm. Previous work has shown that NEs penetrate through hair follicles and skin pores to significant levels in both the epidermis and dermis. Three NEs were evaluated against 9 gram-positive species.

Methods: MICs (broth microdilution) and MBCs were determined using CLSI standard methods.

Results: W205EC, P4075EC and W205GBA2ED had MIC90s ranging to 220 μg/mL for each of the species of 1-16, 2-16 and 4-16 μg/mL, respectively, including organisms that were resistant to topical and systemic antimicrobials. MICs were for 35 isolates: W205EC was iodatal against all isolates while W205EC and P4075EC were iodatal against 94% of isolates.

Conclusions: The antimicrobial spectrum and potency of NEs, and their ability to permeate epidermal and dermal tissues, make them ideal candidates for treatment of superficial skin and soft tissue infections caused by leading gram-positive pathogens, including MRSA.

RESULTS

Table 1. Susceptibility of nine gram-positive isolates to these nanoemulsions and comparator.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Enterococcus faecium</th>
<th>Enterococcus faecalis</th>
<th>Staphylococcus aureus</th>
<th>Staphylococcus epidermidis</th>
<th>Staphylococcus simulans</th>
<th>Staphylococcus haemolyticus</th>
<th>Staphylococcus intermedius</th>
<th>Streptococcus pyogenes</th>
<th>Streptococcus mitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>W205EC</td>
<td>0.5 – &gt;16</td>
<td>0.5 – &gt;8</td>
<td>&gt;2 – &gt;16</td>
<td>0.5 – &gt;16</td>
<td>&gt;2 – &gt;16</td>
<td>&gt;2 – &gt;16</td>
<td>&gt;2 – &gt;16</td>
<td>&gt;2 – &gt;16</td>
<td>&gt;2 – &gt;16</td>
</tr>
<tr>
<td>P4075EC</td>
<td>0.5 – &gt;16</td>
<td>0.5 – &gt;8</td>
<td>&gt;2 – &gt;16</td>
<td>0.5 – &gt;16</td>
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<tr>
<td>W205GBA2ED</td>
<td>0.5 – &gt;16</td>
<td>0.5 – &gt;8</td>
<td>&gt;2 – &gt;16</td>
<td>0.5 – &gt;16</td>
<td>&gt;2 – &gt;16</td>
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Figure 2. Scanning electron micrographs of M. fraternus W205EC.

Figure 3. SEM micrograph of M. fraternus W205EC 1000 x.

METHODS

Emulsion manufacturing. Nanoemulsions W205EC, P4075EC, and W205GBA2ED are oil-in-water emulsions manufactured from ingredients that are Generally Recognized As Safe (GRAS) with a cationic detergent (cetylpyridinium chloride, CPC), or bencalkonium chloride (BC) as active ingredients that have proven safe for human use. The emulsion is formed from highly purified oil, ethanol, a nonionic surfactant and water. The average nanodroplet size is 150nm for W205EC and 300nm for P4075EC and W205GBA2ED as measured by dynamic light scattering using a Malvern Zetasizer Nano ZS (Malvern Instruments Ltd, Worcestershire, UK).

Source of Isolates. The source of the clinical isolates were bloodstream isolates collected from a patient at the University of Michigan Hospital. All the isolates were from patients who were admitted to the surgical intensive care unit with a diagnosis of MRSA infection.

Table 2. MIC and MBC values against 20 isolates of MRSA community isolates.

Table 3. Cytolytic activity of nanoemulsions against a subset of 15 gram-positive isolates.

CONCLUSIONS

• Nanoemulsions W205EC, P4075EC, and W205GBA2ED have potential for topical use to eliminate carriage and/or treat uSSTIs caused by MRSA, MSSA and Streptococcus pyogenes.

• W205GBA2ED was bactericidal against all isolates while W205EC and P4075EC were bactericidal against 94% of isolates.

• No cross-resistance to any known antibiotic was observed for any of the nanoemulsion antimicrobial agents.