Pharmacokinetics and efficacy of ectolysin P128 in a mouse model of systemic Methicillin Resistant Staphylococcus aureus (MRSA) infection

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Pharmacokinetic characteristics of P128 (Non-compartmental analysis)

Methods: Pharmacokinetics in mice

Healthy female BALB/c mice were administered single intravenous bolus doses of 10, 30 or 60 mg/kg. Blood samples were collected at different time points and concentration of P128 in plasma was determined by ELISA which was in a micorplate format and utilized affinity-purified rabbit anti-P128 polyclonal antibody. Mobile mouse plasma used to dilute samples was screened to ensure absence of interference in the assay. The mean concentration of P128 over time was plotted and PK parameters were estimated using non-compartmental analysis using Phoenix WinNonlin® software.

PK parameters of P128 following single IV doses of 10, 30 and 60 mg/kg in naive BALB/c mice

<table>
<thead>
<tr>
<th>PK parameter</th>
<th>10 mg/kg</th>
<th>30 mg/kg</th>
<th>60 mg/kg</th>
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</thead>
<tbody>
<tr>
<td>Cmax (μg/ml)</td>
<td>0.81</td>
<td>5.5</td>
<td>12.2</td>
</tr>
<tr>
<td>tmax (h)</td>
<td>0.57</td>
<td>1.45</td>
<td>2.23</td>
</tr>
<tr>
<td>AUC(0-τ) (μg-h/ml)</td>
<td>13.8</td>
<td>53.1</td>
<td>223.1</td>
</tr>
<tr>
<td>t1/2 (h)</td>
<td>6.65</td>
<td>12.4</td>
<td>17.8</td>
</tr>
</tbody>
</table>

**Conclusions**

- **PK of P128** was characterized by low systemic clearance and low Vss with long t1/2.
- **P128 showed rapid antibacterial effect.**
- **Comparison of PK and PD time courses showed that rapid bacterial effect was related to dose-dependent increase plasma exposure of P128, and that this anti-bacterial effect persisted through later time points when the circulating P128 concentrations were lower.**
- **P128 is a potential candidate for treatment of MRSA bacteremia as a stand-alone therapy or in combination with SoC antibiotics because of its rapid antibacterial effect and prolonged maintenance of low CFU counts in blood following administration of a single dose.**

**References**


All animal experiments were conducted in accordance with the guidelines of the Institutional Animal Ethics Committee, GangaGen Biotechnologies Pvt Ltd, Bangalore, India. Authors have been listed in alphabetical order.