

In vitro Activity of Novel Compound RG6006 Against Clinical Isolates of *Acinetobacter baumannii-calcoaceticus* complex in the Presence of 20% Human Serum

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Introduction

- RG6006 is the first representative of a novel class of tethered macrocyclic peptide antibiotics active against *Acinetobacter* spp., including carbapenem-resistant *Acinetobacter baumannii-calcoaceticus* complex (ABC) organisms.
- ABC is often multidrug-resistant, presenting serious treatment challenges.
- In this study, we determined the *in vitro* activity of RG6006 against 100 isolates of ABC: 59 clinical isolates from the 2015–2018 SENTRY Antimicrobial Surveillance program and 41 isolates from the CDC Antimicrobial Resistance Bank.

Materials and Methods

- Clinical ABC isolates were collected from hospitalized patients in 50 medical centres from 26 countries.
- Susceptibility testing was performed using broth microdilution with cation-adjusted Mueller-Hinton broth (CAMHB) for the comparators colistin and meropenem.
 - The comparator breakpoints used CLSI/EUCAST (2022) criteria.
- RG6006 minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) were determined in CAMHB + 20% pooled human serum, both non-heat inactivated and heat-inactivated.

Results

- MIC distributions for RG6006 and its comparators plus MBC distributions for RG6006 for all isolates are shown in Table 1 and Figure 1.
- Isolates were mostly carbapenem-resistant, with 73% resistant to meropenem (CLSI/EUCAST). Susceptibility to colistin was 84.0% (EUCAST).
- MIC and MBC distributions for RG6006 and comparators against meropenem-resistant ABC are shown in Table 2, and colistin resistant isolates are shown in Table 3.
- RG6006 activity was not affected by colistin or meropenem resistance (Tables 2 and 3).
- RG6006 was active against ABC isolates, with MIC_{50/90} values of 0.5/1 mg/L in both non-heat inactivated and heat-inactivated serum.
- 93% of isolates were inhibited by 1 mg/L, with an MIC range of 0.015–4 mg/L.
- The MBC_{50/90} values of RG6006 were 1/4 mg/L in both non-heat inactivated and heat-inactivated serum.

Conclusions

- RG6006 tested in the presence of 20% human serum showed potent activity against a challenging set of ABC, including meropenem-resistant and colistin-resistant isolates.
- Activity was similar in non-heat inactivated serum compared to heat-inactivated serum, indicating that human complement does not contribute to compound activity.
- Accordingly, these *in vitro* results support the development of RG6006 as a treatment for infections caused by ABC, including carbapenem-resistant ABC.

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Table 1. Antimicrobial activity of RG6006 in various media, with comparators colistin, and meropenem tested against *Acinetobacter baumannii-calcoaceticus* complex isolates

| Media | RG6006 MIC (mg/L) | RG6006 MBC (mg/L) | Colistin MIC (mg/L) | Colistin MBC (mg/L) | Meropenem MIC (mg/L) | Meropenem MBC (mg/L) |
|----------------------------|-------------------|-------------------|---------------------|---------------------|----------------------|----------------------|
| Non-heat inactivated serum | 0.5 | 1 | 16 | 16 | 16 | 16 |
| Heat-inactivated serum | 0.5 | 1 | 16 | 16 | 16 | 16 |
| Non-heat inactivated CAMHB | 0.5 | 1 | 16 | 16 | 16 | 16 |
| Heat-inactivated CAMHB | 0.5 | 1 | 16 | 16 | 16 | 16 |

References

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