Antibiotic Potential of Synthetic Aziridinomitosenes
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Abstract: Mitomycin C (MC) was first discovered in the 1950s as an antibiotic and has since been used as a chemotherapeutic. MC has been shown to cross-link DNA, resulting in cellular death. Synthetic aziridinomitosenes (AZMs) are structurally similar to MC and have been shown to produce more DNA crosslinks than MC, resulting in potential use as a new cancer treatment. Due to MC’s properties as a potent antibiotic, the synthetic AZMs also have possible use as antibiotics due to their similar structures. MC, an unsubstituted AZM, and a C6-Methyl AZM were tested against various gram positive and gram negative bacteria. Initial results conclude that synthetic AZMs are able to decrease bacterial growth with treatment as low as 1 nM in MRSA. Additional investigations have provided evidence that cell survival is lower in AZM-treated bacteria over MC. Along with reduced survival rate, biofilm production also decreased upon AZM and MC treatment.

Background

• Only two antibiotics have been approved by the FDA since 2008.a
• Antibiotics are most effective when bacteria are in their planktonic, or free-swimming, form; however, bacteria form biofilm.b
• Biofilm production leads to antibiotic resistance in bacteria. b
• Mitomycin C (MC) is a natural anticancer/antibiotic produced by Streptomyces caesipitosus and lavendulae.c
• Aziridinomitosenes (AZMs) are synthetic analogs of MC with varying substitution patterns at C6, C7 and C10.

Mitomycin C

AZM 1

C6 Methyl AZM

C10 Methyl AZM

• AZM 1 is effective against Methicillin-Resistant Staphylococcus aureus-1 (MRSA-1) cells shown by the data in the graphs below.

Hypothesis

• With similar structures to mitomycin C, synthetic aziridinomitosenes will demonstrate antibiotic, as well as anticancer, properties.

Conclusions and Future Work

• AZMs are anticancer drugs can potentially be used as an antibiotic:
  • They are effective against MRSA-1 bacteria.
  • They are effective against gram positive/negative bacteria.
  • They reduce biofilm production.
• Future work will consist of:
  • Treating AZMs on more gram positive bacteria strains
  • Completing growth curves and IC₅₀ value tables.

Acknowledgements

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References


24 Hour Treatment of Bacteria with Aziridinomitosenes and Mitomycin C

E. coli ATCC 8739

K. pneumoniae ATCC 13882

Staph. aureus ATCC 6538

Biofilm Production Reduced in Treated Bacteria versus Untreated Bacteria

Kerby-Bauer Assay Indicates C6 Methyl AZM as Potential Antibiotic Agent

Concentration

10 μM 100 nM 1 nM 10 μM 100 nM 1 nM 10 μM 100 nM 1 nM

E. coli ATCC 8735

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S. aureus ATCC 6738

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