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Antibacterial effects of quaternary bis-phosphonium and ammonium salts of pyridoxine on *Staphylococcus aureus* cells: A single base hitting two distinct targets?

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Abstract

We studied the effects of quaternary bis-phosphonium and bis-ammonium salts of pyridoxine with lipophilic substituents on the survival and morphology of *Staphylococcus aureus* cells. We found that, while originating from the same base, they exhibit considerably different antimicrobial mechanisms. In the presence of Ca^{2+} ions the MIC and MBC values of ammonium salt increased 100-fold, suggesting that Ca^{2+} ions can successfully impede the membrane Ca^{2+} ions exchange required for ammonium salt incorporation. In contrast, in the presence of quaternary phosphonium salt, the artificial capsular-like material was formed around the cells and the filamentous and chain-like growth of the cells was observed suggesting the disruption of the cell division mechanisms. Altogether, both pyridoxine derivatives successfully inhibited the growth of gram-positive bacteria (*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*) and *Escherichia coli* considerably, while demonstrated nearly no effect against *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. We suggest that due to their effects on distinct and likely complementary targets the derivatives of pyridoxine represent potentially perspective antibacterials with complicated adaptation and thus with lower risk of drug resistance development.

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Keywords

Antibacterial activity, Fluorescent microscopy, Pyridoxine, Quaternary ammonium salts, Quaternary phosphonium salts