

MS13-1-2 Study on the crystal structure-antibacterial activity relationship of quaternary ammonium Schiff compounds based on difference in their electrostatic potential
#MS13-1-2

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Abstract

The quaternary ammonium salts (QAS) are interesting class of N-containing organic compounds possessing wide range of applications derived from their unique structural properties - positively charged nitrogen "head" and lipophilic "tail". The amphiphilic nature of QAS, together with the facile synthesis route determine their extensive use as surfactants, phase-transfer catalysts, antimicrobial and bactericidal agents etc.

This work is focused on the synthesis, physicochemical characterization and antibacterial properties of novel aromatic quaternary ammonium compounds derivatives of 4-pyridinecarboxaldehyde containing azomethine bridged aromatic fragments (e.g. Schiff bases). The developing of new quaternary ammonium Schiff bases is an expansion of our previous studies on the antibacterial properties of several QAS derivatives of quinoline (QN) and 4-pyrrolidino pyridine (4-PP) against the bacterial strains of *S. aureus*, *E. Coli*, *K. Pneumoniae* and *P. Aeruginosa* [1, 2]. The results from those studies concluded that QN and 4-PP QAS are predominantly active against the Gram positive bacteria – *S. Aureus* and in addition the antibacterial activity increases significantly with the replacement of the quinoline fragment with 4-pyrrolidino pyridine (Fig. 1a). The detailed analysis of the crystal structures of the studied compounds revealed that the drastic change in the antibacterial effect could be connected to the different properties of the 4-pyrrolidino pyridine and quinoline fragments but also could be related to variances in the electron density distribution in the molecule. Indeed, the calculated electrostatic potential [3] of the inactive/active pair of quaternary ammonium compounds (Fig. 1b) points out towards significant differences in the electron density distribution. One can notice that the molecule of the inactive quinoline derivative is predominantly positively charged whereas the active 4-pyrrolidino pyridine derivative is in the form of dipole. From these findings it was clear that in order to further enhance the antibacterial effect of the studied QAS and/or to expand the possible bacterial targets, it is important to maintain the separation of the opposite charges in the molecule. Following this logic, new aromatic fragments bearing different functional groups with positive or negative induction effects (I^+ or I^-) were bonded to the main quaternary ammonium molecule via azomethine bridge (Fig. 1c). The electrostatic potential of the obtained quaternary ammonium Schiff compounds was calculated from their respective crystal structures. The synthesized compounds showed increased antibacterial activity towards *S. Aureus* with lower MIC values.

Acknowledgements: This work was supported by the Bulgarian Science Fund (project contract КП-06-M59/7).

References

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