GREEN ACCELERATED SYNTHESIS OF ANTIMICROBIAL QUATERNARY AMMONIUM SALTS

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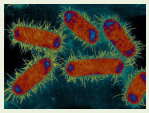
Abstract

It has been demonstrated that pathogenic microorganisms are resistant to the action of disinfectants and some antibiotics. Therefore, the identification of new sources of antimicrobial compounds has presently become a hot topic. Quaternary ammonium salts (QAs) are known as one of the most visible and effective classes of disinfectants for nearly a century.[1] With various structures, QAs were obtained using different approaches, and exhibited different antimicrobial activities and potential applications.[2] The aim of this study was to synthesize and evaluate the antibacterial potential of quaternary ammonium salts, bearing pyridinium cores, against pathogenic bacteria. The antibacterial activity of the QAs against *Escherichia coli* was explored by determining the minimum inhibitory concentration (MIC). The viability of aerobic bacteria was determinated with the Tetrazolium/Formazan Test, a method that was found to be the best alternative approach. The antibacterial potential of quaternary ammonium salts was followed for 24 h and, in this way, the MIC values were confirmed as the concentrations of quaternary salts that inhibited the bacterial growth.

Objectives

- **Synthesis and characterization** of 25 pyridinium quaternary salts, QAs, by microwaves and ultrsounds-promoted reaction.
- **Determination of antimicrobial activity** through ***agar diffusion method and MTT*** *(3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide)* ***assay against E. coli***



Materials and methods

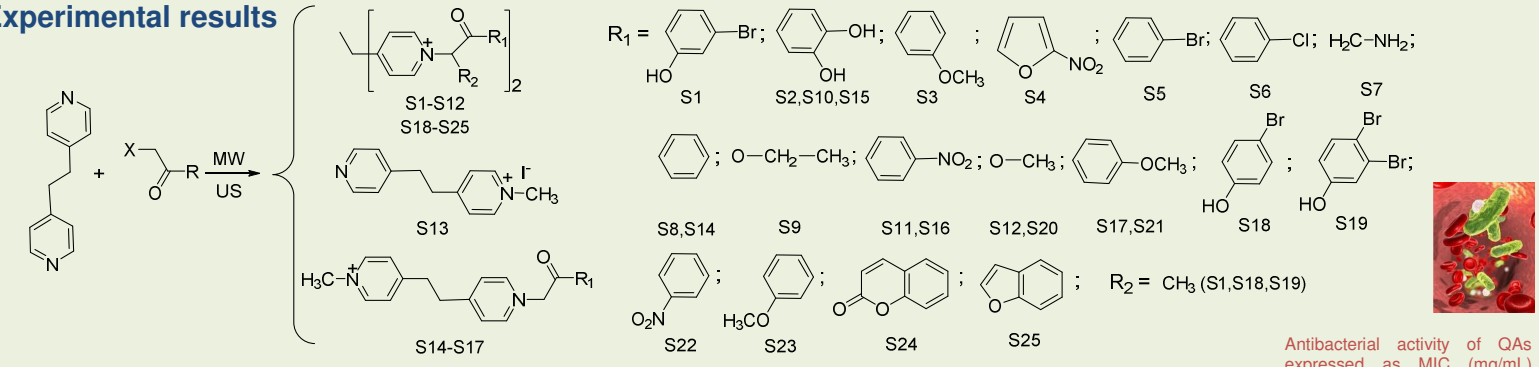
Synthesis: A typical procedure involves irradiation of a mixture of 1 equiv of pyridine derivatives and 1 equiv of halide derivatives using acetonitrile as solvent under microwave irradiation for 5–10 min and ultrasounds for 1h. At the end of the reaction, the salts were recovered by simply adding them into acetonitrile, thus allowing their filtration.

Bacterial strain: The pathogenic bacteria, Escherichia coli ATCC 25922 (clinical isolate), used as test microorganism for antibacterial activity study, was collected from the Microbial Culture Collection, Sf. Andrei Hospital, Galati, Romania.

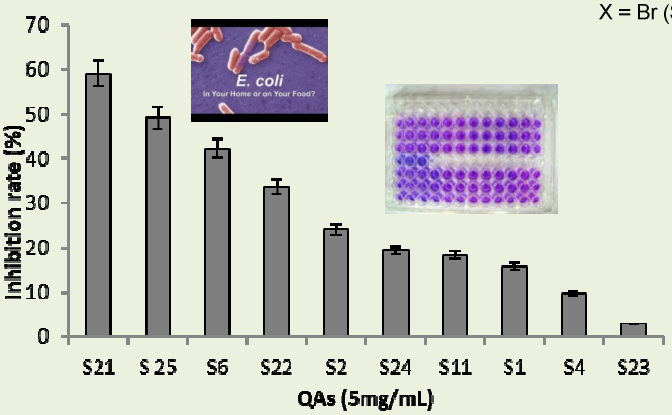
Antibacterial activity evaluation by Tetrazolium/Formazan test: The TTC test was evaluated as a qualitative antibacterial method using a Microplate Spectrophotometer (NanoQuant, Tecan) at 570 nm.

Minimum inhibitory concentration (MIC) determination: was defined as the lowest concentration of QAs that inhibit the growth of bacteria in a microdilution well plate.

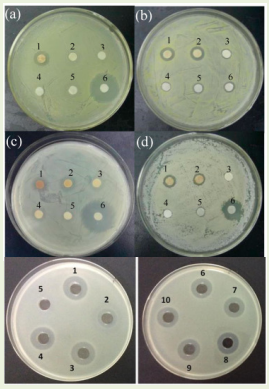
Experimental results



X = Br (S1,S3-S5,S7-S11,S18-S25); Cl (S2,S6,S12); I (S13-S17)



Inhibition rate (%) of E.coli by QAs determined by Tetrazolium/Formazan Test



Antibacterial activity of QAs expressed as MIC (mg/mL) determined by the microdilution method against E.coli

QAs	Minimum inhibitory concentrations (MICs) (mg/mL)
S21	0.312
S25	0.312
S6	0.312
S22	0.625
S2	0.625
S24	0.625
S11	1.25
S1	1.25
S4	2.5
S23	2.5

Conclusions

- ✓ We have developed an operationally simple and efficient method for the synthesis of pyridinium quaternary salts by microwave and ultrasounds promoted reaction.
- ✓ The conditions employed furnished good yields than by conventional heating methods.
- ✓ These results confirm the applicability of microwave and ultrasounds heating to the improvement of classic reactions.
- ✓ We found that the most QAs have reasonable activity against E.coli. A significantly antibacterial activity was found to S22,S2 and S24. The most active QAs were S21,S25 and S6 having MIC value of 0.312 mg/mL against E.coli.

References

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2. Yan, X.; Huining, X.; Yi, Z., *Int. J. Mol. Sci.* **2015**, *16*, 3626-3655.

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