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*As a manuscript*

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**Formation and antibiotic resistance of bacterial biofilms**

***Methylophilus quaylei* and its isogenic streptomycin-resistant mutant**

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**Dissertation**

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## Abstract

- This study aimed to the creation of new bacterial biofilm inhibition systems based on the combination of different antibiotics with sodium oleate and biogenic silver nanoparticles (SNPs) using an aerobic methylotrophic bacterium *Methylophilus quaylei*.
- The biofilm was developed by *Methylophilus quaylei* on hydrophobic materials – Teflon and polypropylene – and was studied by colony-forming units (CFU) counting, staining with crystalline violet, light, transmission and scanning electron microscopy.
- The inhibitory effect of different antibiotics ampicillin, kanamycin, rifampicin, streptomycin, polymyxin B on the biofilm and planktonic forms of *Methylophilus quaylei* was tested.
- The effect of exogenous sodium oleate on biofilm growth of *Methylophilus quaylei* and the morphology of biofilms both as a single additive and in combination with antibiotics and SNPs was tested.
- Biogenic silver nanoparticles (SNPs) using *Methylophilus quaylei* were obtained then were tested on the growth of bacterial biofilms.
- A Comparative analysis of planktonic growth characteristics and biofilm forms of *Methylophilus quaylei* in the presence of exogenous sodium oleate showed that sodium oleate does not inhibit the growth of the planktonic form but reduces biofilm growth and enhances the bactericidal effect of the antibiotics ampicillin and kanamycin and SNPs when used in combinations.
- For the first time, methylotrophic bacteria were used for the preparative production of biogenic (SNPs). The ability to reduce silver ions was obtained by cell-free culture fluid of *Methylophilus quaylei* MT. The conditions for the biosynthesis of cubic SNPs with an average size of 38 nm

- The effect of exogenous sodium oleate on the biofilm growth of *Methylophilus quaylei* and the morphology of biofilms was studied both as a single additive and in combination with antibiotics and SNPs. A synergistic bactericidal effect of sodium oleate in combination with antibiotics and SNPs was found.
- The effect of SNPs on bacterial growth in biofilms has been studied. A dose-dependent bactericidal effect of SNPs was detected. SNPs in combination with sodium oleate had the greatest anti-biofilm effect.
- Changes in the structure of biofilms and cell surfaces in the presence of exogenous sodium oleate, alone or in combination with antibiotics and SNPs, have been studied by light and scanning electron microscopy. The addition of sodium oleate to the formed biofilms in combination with antibiotics and SNPs leads to a change in the architecture of biofilms, a decrease in the amount of matrix, an increase in porosity leading to a complete destruction of the biofilm structure.
- An anti-biofilm effect of polymyxin B and an increasing in the sensitivity of the streptomycin-resistant mutant strain of *M. quaylei* SM to streptomycin in the presence of polymyxin B were detected, both in biofilms and in the planktonic form.