EV0443
ePoster Viewing
Resistance mechanisms

In vitro effect of deferoxamine on the efficiency of metronidazole against Capnocytophaga spp.

Zohreh Tamanai-Shacoori[1], Elodie Ehrmann[2], Olivier Loreal[3], Oliviero Nolwenn[4], Martine Bonnaure[5], Anne Jolivet-Gougeon*[6]

[1]*Université Rennes 1, Ea 1254 Microbiologie, Rennes, France*

[2]*Faculté D'odontologie, Université de Nice-Sophia-Antipolis, Nice, France*

[3]*Inserm U991, Rennes, France*

[4]*Université de Rennes 1, Rennes, France*

[5]*Faculté D'odontologie, Ea 1254 Microbiologie, Rennes, France*

[6]*Teaching Hospital, Pontchaillou, Biology/Bacteriology, Ea 1254 Microbiologie, Rennes, France*

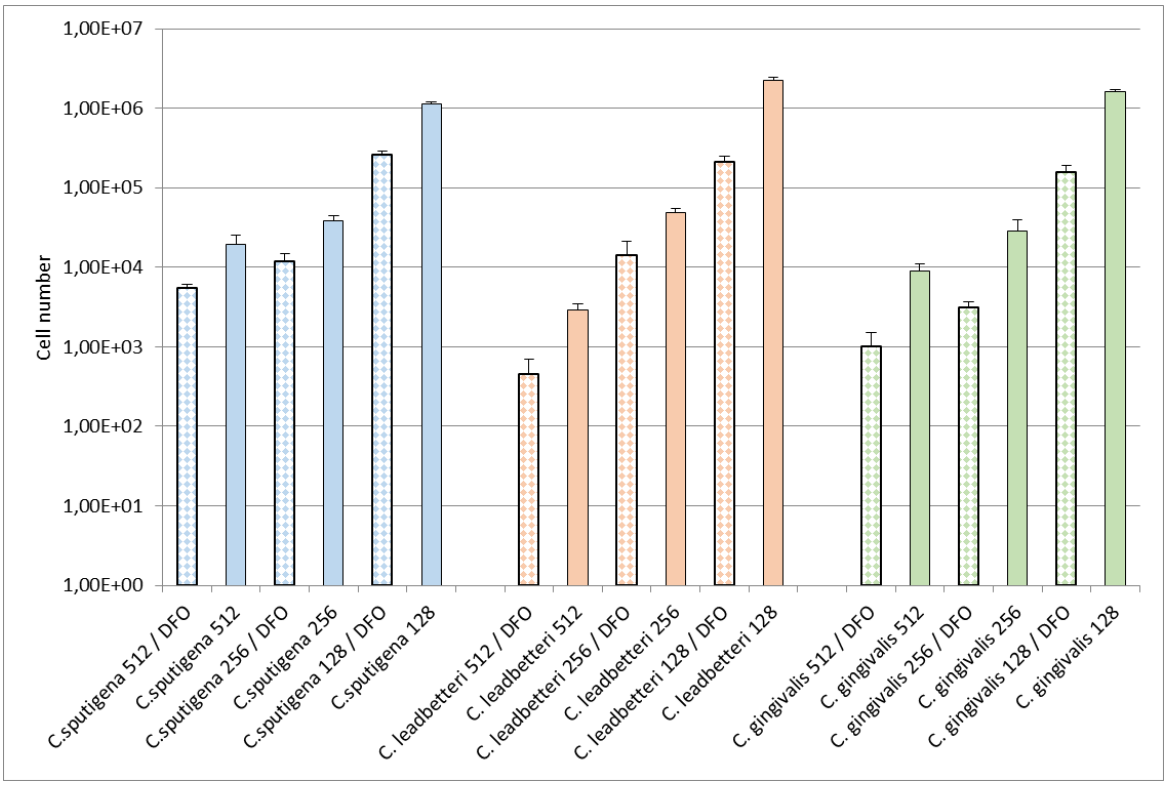
Background: For successful proliferation in multicellular organisms, microbial pathogens must possess ability to acquire growth-essential iron from their hosts. Deferoxamine (DFO), a FDA-approved iron chelator, has been extensively used for parenteral chelation therapy in iron-overloaded states, especially during thalassemia. *Capnocytophaga* spp. are normal anaerobic inhabitants of the oropharyngeal flora, but may be involved in periodontal and systemic diseases. Metronidazole, a 5-nitroimidazole, has been regarded as an important therapeutic agent in the treatment of anaerobic infections. Recent data show an emergence of resistance in *Capnocytophaga* spp. against antimicrobial agents, including metronidazole. The aim of this study was to investigate whether the exposure to DFO may increase susceptibility of *Capnocytophaga* spp. to metronidazole.

Material/methods: *Capnocytophaga* cells (OD_{600}≈0,1) were primary incubated in serial dilutions of DFO (0–0.24 mM) in brain heart infusion broth enriched with yeast extract (0.5%), hemin (5 µg mL^{-1}) and vitamin K1 (1 µg mL^{-1}) (BHIe). Cells viability was determined by OD_{600nm} measurement in anaerobic conditions at 37°C after 24h. Threefold serial dilutions of metronidazole (128, 256, 512 mg L^{-1}) were prepared in BHIe, with or without 0.24mM DFO. *Capnocytophaga* cells inoculated (10^7 cells mL^{-1}) into the media were enumerated after 24h in anaerobic condition at 37 °C.

Results: The viability of three metronidazole resistant *Capnocytophaga* strains (*C. sputigena, C. gingivalis* and *C. leadbetteri* with MICs > 128mgL^{-1}) was not affected by 0.24 mM DFO. The effect of 0.24mM DFO on the efficiency of metronidazole was evaluated on these strains. Antibacterial properties of three concentrations of metronidazole tested (128, 256, 512 mg L^{-1}) against *Capnocytophaga* increased in the presence of DFO, as shown by survival curves in absence and presence of DFO.

Conclusions: Further investigations are required to better understand the mechanisms of action of DFO and other iron chelators. Their use could be an adjunctive therapeutic agent against periodontal disease.

Fig.1. Cell number of *Capnocytophaga* spp. exposed to metronidazole (128, 256 and 512 mgL^{-1}) for 24h, in the presence or absence of DFO (0.24mM).


1,00E+07
1,00E+06
1,00E+05
1,00E+04
1,00E+03
1,00E+02
1,00E+01
1,00E+00
Cell number
C.sputigena 512 / DFO
C.sputigena 512
C.sputigena 256 / DFO
C.sputigena 256
C.sputigena 128 / DFO
C.sputigena 128
C. leadbetteri 512 / DFO
C. leadbetteri 512
C. leadbetteri 256 / DFO
C. leadbetteri 256
C. leadbetteri 128 / DFO
C. leadbetteri 128
C. gingivalis 512 / DFO
C. gingivalis 512
C. gingivalis 256 / DFO
C. gingivalis 256
C. gingivalis 128 / DFO
C. gingivalis 128