Unravelling the anti-biofilm effects of plant derived compounds and nanoparticles at sub-lethal concentrations

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Aim of the PhD project

The aim of this PhD project is to develop innovative biocide-free anti-biofilm strategies based on nanoparticles (NPs) and plant-derived compounds at sub-lethal concentrations

The use of sub-lethal doses of natural molecules and NPs offers an elegant way to interfere with specific key-steps that orchestrate biofilm formation (**Fig.1**), disarming microorganisms without affecting their existence, sidestepping drug resistance and extending the efficacy of the current arsenal of antimicrobial agents.

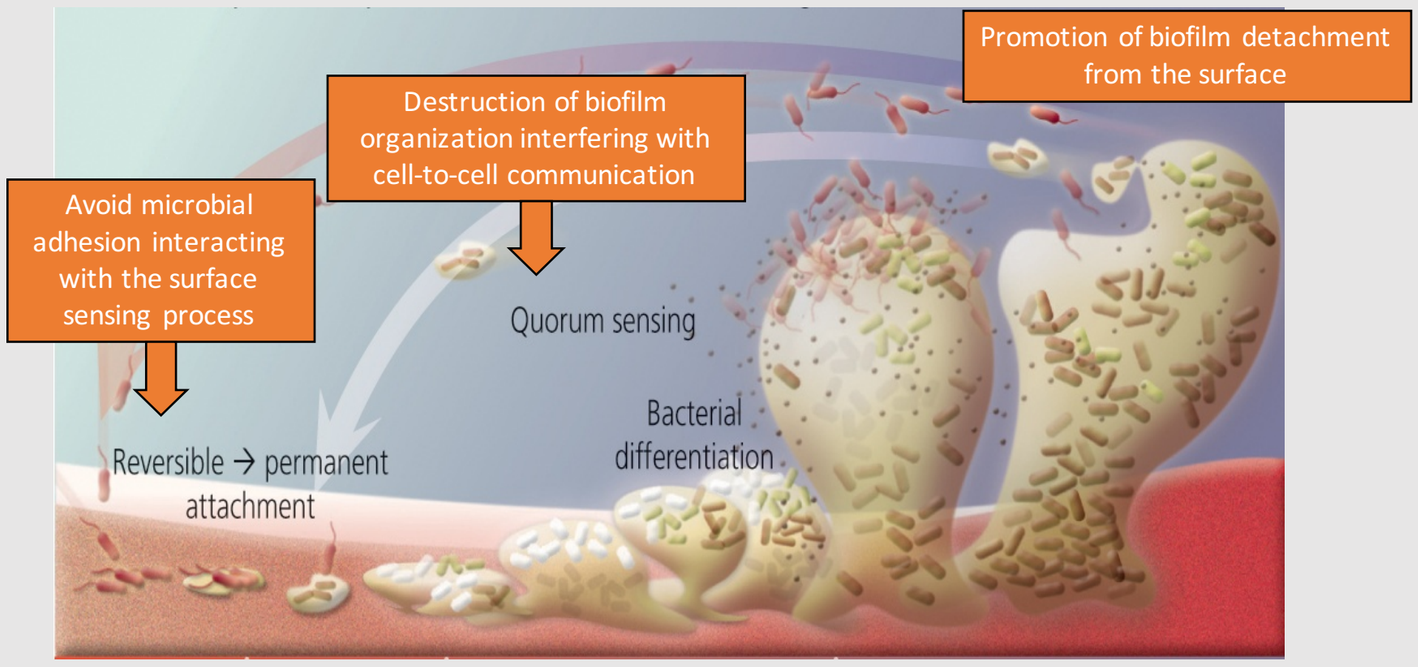

Fig. 1. The biofilm life cycle and different modes of action of some anti-biofilm compounds at sub-lethal concentrations [1].

State of the art and model systems

The worldwide safety is seriously jeopardized by the spread of microorganisms in form of biofilm, a microbial community attached to a surface and embedded in a matrix of extracellular polymeric substances. Biofilm cells exhibit an altered phenotype with respect to growth rate and gene transcription of planktonic cells [2]. **Biofilms can be detrimental in different domains** because biofilms demostrated higher resistance and resilience to antimicrobial treatments than their planktonic couterpart.

New anti-biofilm strategies with novel targets and modes of action should have advantages over known biocides. Following this trend, the use of mechanisms subtler than the killing activity, like those influencing the biofilm behavior (e.g. adhesion, cell-to-cell communication, motility, dispersion), would offer alternative approaches [3].

NPs and some plant-derived compounds are known to affect oxidative stress [5]. Starting from the assumption that reactive oxydative species (ROS) act as signalling molecules affecting biofiom formation [3, 4], we could envision a new line of anti-biofilm startegies based on oxidative stress regulation. Thus, we will use NPs and plant-derived compounds at sublethal concentrations to provide sub-inhibitory levels of ROS with the final goal of modulating biofilm genesis.

Two main systems (**Fig.2 a, b, c**) will be used as tools to modulate oxidative stress homeostasis in biofilm-forming microorganisms:

- **Seagrasses and mangroves**: by growing in highly saline conditions it is predicted that these groups may possess some rare and new flavonoids and phenolic acids with anti-oxidant properties [6].
- **Metallic NPs** are materials with dimension below 100 nm. They exhibit many fascinating properties due to their size and through several methods is possible to obtain high amount of metallic NPs, controlling the size, shape, and structure [7].

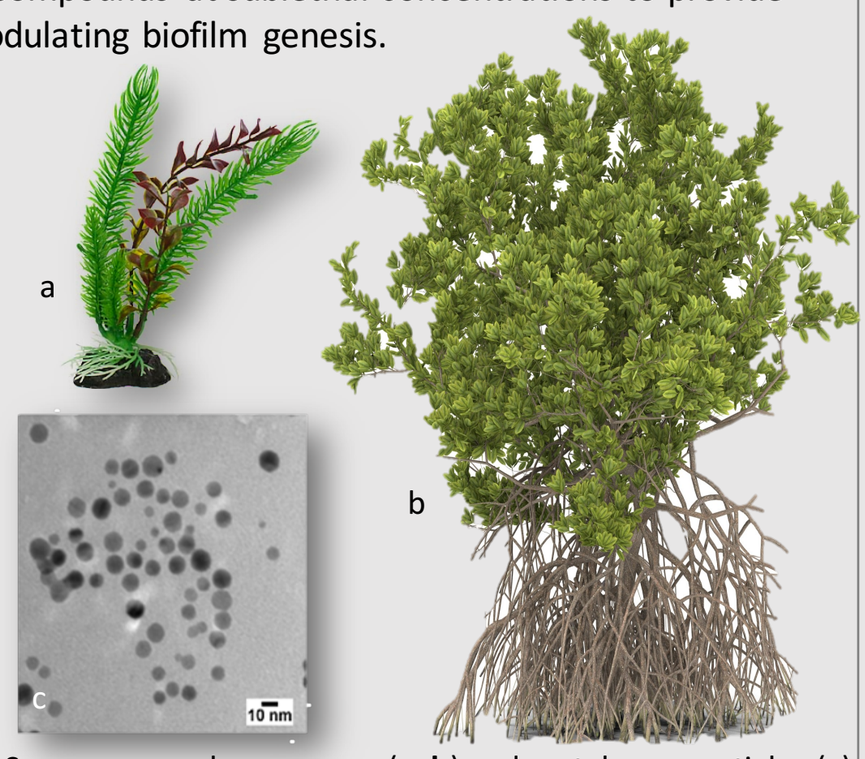

Fig.2 Seagrasses and mangroves (**a**, **b**) and metal nanoparticles (**c**)

These observations make halophytes and NPs promising source for developing non-biocidal anti-biofilm strategies.

Steps of the research

- Identification of sub-lethal concentrations of plant extracts and NPs using model bacteria and fungi.
- Assess the effects of the selected plant extract fractions and NPs at sub-lethal concentrations on:
  i) cell adhesion
  ii) biofilm structural development.
- Study the mechanism of action of the selected plant extract fractions and NPs at sub-lethal concentrations (targets, physiological perturbation etc).

Collaboration

This PhD project will be carried out in collaboration with the Institute of Botany of the Leibniz University of Hannover (Germany).

References

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