Synthesis of new benzimidazole derivatives and evaluation of their biological activity as bacterial flocculating agents

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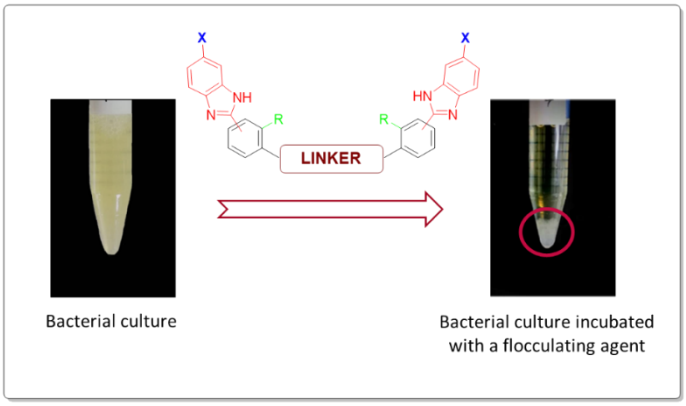
Bacterial flocculation is a biological phenomenon that has shown an increasing interest in recent years due to its various applications, ranging from wastewater treatment to biodegradation or biocatalytic processes. During this phenomenon, bacterial cells form eye-visible flocs. This process can be observed naturally but can also be provoked by the use of flocculating agents[1]. The mechanism of action of the existing agents is mainly based on electrostatic interactions between the positive charge carried by these systems and the negatively charged bacterial membranes[2]. However, this specific mechanism of action, combined with high cost and toxicity are constraints preventing the use of the current flocculating agents on an industrial scale[1].

As the benzimidazole moiety is found in many structures exhibiting interesting pharmacological activity (such as anti-viral, anti-fungal or even anti-bacterial agents[3]), our work focused on the development of new heterocyclic derivatives bearing benzimidazole units. In recent studies, we have highlighted that some of these heterocyclic structures exhibit an important activity against both Gram (+) and Gram (-) bacterial strains characterized by the rapid appearance (within a few minutes) of flocs when the bacterial suspension is incubated with a low concentration of derivative.



Interestingly, the synthesis and evaluation of this chemical library allowed to highlight given structural criteria essential for the expression of the flocculation activity. Moreover, the structure of the evaluated heterocycles suggests a non-conventional mechanism of action when compared to classical "positively-charged" flocculating agents. To go further into the comprehension of the observed phenomenon, we decided to carry out some additional studies including scanning electron microscopy (SEM) and metabolomic experiments alongside with other biological characterizations of the bacterial flocs.

References:

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3. Pullagura, M. K. P., *et al*. Potent Biological Agent Benzimidazole - A review. *Int. J. Pharm. Pharm. Sci.* **8**, 22 (2016).