

21570 | The action of selected natural products as antibiotic resistance modifiers and biofilm control agents

Francisca Massano^{1,2}; Mariana Sousa^{1,2}; Anabela Borges^{1,2}; Manuel Simões^{1,2}

LEPABE - Laboratory for Process Engineering, Environment, Biotechnology and Energy, Faculty of Engineering, University of Porto, Porto, Portugal¹; ALiCE - Associate Laboratory in Chemical Engineering, Faculty of Engineering, University of Porto, Porto, Portugal²

Background & Aim: The rising threat of multidrug-resistant bacteria, especially in biofilms, demands innovative and efficient treatment strategies. Therefore, this study aimed to assess the antibiofilm and antibiotic resistance-modifying potential of natural compounds, such as phytochemicals and natural deep eutectic solvents (NADES). **Methods:** *In vitro* assays were conducted using two monoterpenes (menthol and linalool) and a choline chloride-raffinose NADES in combination with ten antibiotics (methicillin, amoxicillin, oxacillin, erythromycin, ciprofloxacin, mupirocin, fusidic acid, tetracycline, tobramycin, and gentamicin) against *Escherichia coli* CETC 102 and *Staphylococcus epidermidis* ATCC 35984. Minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) were determined for the phytochemicals. Disc diffusion was used to evaluate bacterial susceptibility to antibiotics and the potential of the dual combinations. Biofilm control efficacy was assessed through biomass and metabolic activity quantification, along with cell culturability. **Results:** Menthol displayed a MIC and MBC of 800 µg/mL against *E. coli* and an equivalent MIC against *S. epidermidis*. Linalool exhibited a MIC of 800 and 400 µg/mL against *E. coli* and *S. epidermidis*, respectively. Disc diffusion indicated a potentiation effect of both molecules on erythromycin against *E. coli*, and of menthol on amoxicillin against *S. epidermidis*. Biofilm control studies showed that both molecules applied individually reduced more than 90% of the biofilm's metabolic activity, yielding, in some cases, a total reduction of culturable cells. Moreover, the dual combinations with antibiotics enhanced their activity up to 40% in biofilm metabolic inactivation, 13% in biomass removal, and 2.8 logs in culturability reduction. **Conclusions:** This study has revealed promising results, showing the potential of these terpenes and NADES as antibiotic resistance modifiers and supporting menthol and linalool as strong antibiofilm agents.

Keywords: Antibiotics, Antimicrobial Resistance, Phytochemicals, Natural Deep Eutectic Solvents, Biofilms.

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