20629 | Antimicrobial and antibiofilm effect of phytochemicals as a potential treatment against healthcare-associated infections

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Abstract

The treatment of bacterial infections has been troubled by the increased resistance to antibiotics [1, 2]. Thus, it is crucial to discover novel and effective therapies to control and eradicate planktonic and sessile bacterial cells [3]. Phytochemicals have demonstrated broad-spectrum and effective antibacterial effects as well as antibiotic resistance-modifying activity [4]. In this study, perillyl alcohol and hydrocinnamic acid were characterized for their antimicrobial and antibiofilm action against *Escherichia coli* CECT 434. Furthermore, dual and triple combinations of these phytochemicals with chloramphenicol and amoxicillin were investigated for the first time. Perillyl alcohol had a minimum inhibitory concentration (MIC) of 256 µg/mL and a minimum bactericidal concentration (MBC) of 512 µg/mL. Hydrocinnamic acid had a MIC of 2048 µg/mL and an MBC > 2048 µg/mL. Checkerboard demonstrated synergism or additive effects for chloramphenicol/perillyl alcohol, chloramphenicol/hydrocinnamic acid, and amoxicillin/hydrocinnamic acid. The analysis with Combenefit showed synergism for various concentrations of amoxicillin with each phytochemical and mainly at low concentrations of

chloramphenicol. Regarding the biofilms, both phytochemicals provided a total elimination of colony-forming units (CFU), for 5×MIC and 10×MIC. The highest percentages of metabolic inactivation (88.5% ± 0.8% for 10×MIC) and biomass reduction (61.7% ± 1.6% for 10×MIC) were obtained for *E. coli* treated with amoxicillin. All combinations resulted in high efficacy concerning metabolic inactivation and revealed moderate efficacy in terms of biomass reduction. Considering the culturability of sessile cells, synergism was determined for 20.0% of combinations, additivity for 60.0%, and indifference for 20.0%. The results of this study highlighted the potential of combinatorial therapies for microbial and biofilm control, where phytochemicals play an important role as resistance-modifying agents.

Keywords: Antibiotic recalcitrance; Biofilm eradication; *E. coli* infections; Plant-based natural product; Combinatorial therapy; Phytochemical-antibiotic interaction.

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