

Exploring wine industry by-products for targeting *Staphylococcus aureus* in diabetic foot infections

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Abstract

Diabetic foot infections are a serious complication associated with diabetes mellitus disease. They are usually polymicrobial infections, being *Staphylococcus aureus* the most frequent microorganism. This microorganism has several resistance mechanisms and virulence factors, leading to high resistance to antibiotics. The main goal of this study was the valorisation of winemaking industry residues as antibiotic adjuvants, motivated by this serious situation and the need for alternative antimicrobial strategies. For that, firstly, extracts of red grape pomace (RPE) were prepared from different red grape varieties provided by SOGRAPE VINHOS SA, obtaining extraction yields from 4 to 30%. After that, the antimicrobial activity and the mode of action of the RPE aqueous and hydroethanolic (50:50 v/v-ET50;70:30 v/v-ET70) were studied by microdilution and modified disc-diffusion methods; and by an evaluation of propidium iodine (PI) absorption, intracellular potassium (K⁺) leakage and virulence factors production, respectively. Additionally, the antioxidant potential of the RPE was also tested. The antibacterial activity against *S. aureus* was confirmed once MIC values of 25 mg/mL and 50 mg/mL were obtained for the *S. aureus* strains under study (CECT976 and RN4220). However, the MBC value of 25 mg/mL was obtained only for the *S. aureus* CECT976 strain. Preliminary tests to analyse the synergic potential of RPE with antibiotics showed a potentiation effect in different combinations. An antioxidant effect was detected for the ET50 and not detectable for the ET70. After exposure to the RPE, *S. aureus* showed permeabilization to PI, leakage of intracellular K⁺ for RN4220 strain, but not for CECT976. Regarding RPE effect on proteases and gelatinases production, no conclusions were obtained, and for the production of siderophores it was possible to verify an increase when RPE were present. Overall, RPE's antibacterial and antioxidant effects were found to be promising.