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Essential oils from *Ocotea diospyrifolia* and *Ocotea velloziana*: Chemical composition and evaluation of antimicrobial activity against resistant *Klebsiella pneumoniae*

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Palavras Chave: *Essential oil; Ocotea; Polymyxin B; Antimicrobial resistance; Multi-drug resistance; Synergistic interactions.*

Highlights

Essential oils from *Ocotea diospyrifolia* and *Ocotea velloziana*: Chemical composition and evaluation of antimicrobial activity against resistant Klebsiella pneumoniae. Given that the threat posed by AMR is increasing, the development of alternative antimicrobial therapeutic techniques has become crucial. Therefore, many researchers consider the application of natural compounds, such as plant EOs, and their combination with antibiotics as a promising approach to combat multidrug-resistant bacteria.

Resumo/Abstract

Antimicrobial resistance, particularly in carbapenem-polymyxin-resistant *Klebsiella pneumoniae* (CPR-Kp), is a major challenge associated with severe infections (1). In this study, we assessed the chemical composition and antimicrobial properties of essential oils (EOs) from *Ocotea diospyrifolia* (OdEO) and *Ocotea velloziana* (OvEO) against CPR-Kp. The EOs were extracted from the leaves via hydrodistillation and analyzed using gas chromatography-mass spectrometry. The antimicrobial activities of the EOs, alone and along with polymyxin B (OdEO-PMB and OvEO-PMB), were assessed through checkerboard assays, survival curves, and biofilm inhibition. Cell membrane permeability, reactive oxygen species levels, and scanning electron microscopy (SEM) were used to investigate antimicrobial mechanisms. Safety was evaluated by conducting hemolysis and toxicity tests in *Caenorhabditis elegans*. An in vivo infection model was constructed using *C. elegans* larvae to assess survival rates. OdEO and OvEO exhibited distinct chemical compositions, with α-bisabolol and viridiflorene as the major components, respectively. In silico analyses revealed that OdEO components can modulate the porin OmpK36, suggesting their ability to serve as antibiotic adjuvants. OdEO-PMB and OvEO-PMB reduced the PMB concentration required to inhibit CPR-Kp growth by 32-fold. Both combinations inhibited biofilm formation and caused bacterial death. The OdEO-PMB combination induced oxidative stress and increased protein leakage. Both treatments were non-toxic and non-hemolytic in the assay performed. In the infection models, OdEO-PMB and OvEO-PMB improved *C. elegans* survival rates to 72.4% and 50.9%, respectively. These results indicated that the Ocotea essential oils investigated are effective adjuvants for PMB, suggesting that they can be used to develop novel therapeutic strategies against CPR-Kp strains.

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