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METABOLOMICS REVEALS THE IMPACT OF SEASONAL VARIATION ON THE CHEMICAL PROFILE AND ANTI-INFLAMMATORY ACTIVITY OF OCOTEA ODORIFERA (VELL.) ROHWER ESSENTIAL OILS

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Ocotea odorifera, commonly known as sassafras or canela-sassafras, has long been used in Brazilian traditional medicine to treat ailments such as edema, gastrointestinal disorders, arthritis, syphilis, and fever. Beyond its ethnopharmacological significance, the species has demonstrated scientifically validated antioxidant, antimicrobial, antimutagenic, and more recently, anti-inflammatory properties[1]. In this study, a metabolomics-driven approach was employed to investigate, for the first time, how seasonal variation shapes both the chemical composition and the anti-inflammatory activity of *O. odorifera* essential oils. Leaves were collected monthly over one year, and essential oils were extracted via hydrodistillation. Gas Chromatography-Mass Spectrometry (GC-MS) analysis revealed pronounced seasonal shifts in composition, with safrole consistently dominant yet variable in concentration levels (55-80%), alongside less abundant constituents such as camphor (4-9%), followed by bicyclogermacrene (2-7%). The essential oils were assessed using an *ex vivo* anti-inflammatory assay, measuring prostaglandin E_2 (PGE_2) levels in lipopolysaccharide-stimulated human whole blood. Ultra-Performance Liquid Chromatography coupled with Tandem Mass Spectrometry (UPLC-MS/MS) was employed to determine PGE_2 inhibition levels. Untargeted metabolomics demonstrated that oils harvested in autumn and spring exhibited fluctuations in the chemical composition, which favored greater PGE_2 inhibition levels compared to those samples from summer. However, the OPLS-DA model reveled β-pinene, limonene, and sabinene as statistically significant variables, all negatively correlated with increased anti-inflammatory activity (VIP > 1; $p < 0.05$; $q < 0.05$). While 4-terpineol and α-cadinol also exhibited high variance important in projection (VIP) scores, and positive correlation, indicating potential biological relevance. However, they did not reach statistical significance threshold, likely due to the limited sample size. These findings highlight how seasonal variations influence the specialized metabolism and anti-inflammatory properties of *O. odorifera* essential oils, providing valuable insights into their therapeutic potential.

Keywords: *Ocotea odorifera, Canela-sassafras, seasonal variation, GC-MS, UPLC-MS/MS, Prostaglandin E_2.*

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