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ECOLOGICAL INTERACTIONS AS DISCOVERY TOOLS: CO-CULTIVATION OF ENDOPHYTIC AND PATHOGENIC PERSIMMON FUNGI IN SEARCH FOR BIOCONTROL AGENTS

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Plant diseases cause annual losses of up to 15% of major global crops, of which about 80% are attributed to pathogenic fungi. The chemical agents traditionally used for pest control have proven unsustainable, being one of the main causes of environmental degradation. Reduced agricultural productivity and excessive agrochemical use, combined with rapid population growth, have put food security at risk. In this context, sustainable strategies such as biocontrol agents emerge as promising alternatives. Endophytic fungi are valuable resources for discovering new natural products, and the co-cultivation strategy enables activation of silent biosynthetic genes, mimicking natural microbial interactions and yielding antifungal metabolites not observed under standard conditions. This study evaluated the antifungal activity of crude extracts from co-cultures of the endophytic fungus *Lasiodiplodia* sp. (EC1), isolated from persimmon (*Diospyros kaki*), and four phytopathogens of the same fruit (*Lasiodiplodia* sp. PC3, *Fusarium* sp. PC4, *Penicillium* sp. PC5, and *Neopestalotiopsis* sp. PC6), in rice medium. Cultures (axenic and co-cultures) were extracted with ethyl acetate and fractionated by vacuum liquid chromatography to remove rice triglycerides. The methanolic fraction (0.5 mg/mL) was tested in agar dilution assays in triplicate. Results showed that axenic RP4 extract inhibited EC1 (85.67 ± 7.86), while co-culture RE1,P4 inhibited EC1 (86.13 ± 3.37) and PC4 (88.20 ± 1.48). Co-culture RE1,P6 was active against EC1 (56.05 ± 4.45) and PC6 (62.10 ± 1.10). Extracts with inhibition above 50% (RE1,P4 and RE1,P6) were analyzed by UHPLC-MS/MS and ^{1}H NMR for chemical profiling. Mass data were pre-processed in MZmine (v4.7.3), and molecular networking in GNPS2 revealed exclusive and shared metabolites, including epiquisetine, polanrazine B, and lasiodiplodin. These extracts will undergo further purification and structural characterization by ^{1}H NMR and LC-MS/MS. Overall, the findings highlight endophytic–phytopathogen co-cultivation as a promising strategy for prospecting antifungal metabolites with potential biocontrol applications, contributing to sustainable agriculture. The authors thank the support from their institutions and the financial support of FAPESP scholarship #2024/01273-5.

Keywords: *fungi; persimmon; antifungal activity; co-cultivation; molecular networking.*