High-throughput metabolomics reveals dysregulation of hydrophobic metabolomes in cancer cell lines by *Eleusine indica*

ABSTRACT

Eleusine indica, which is used in traditional medicine, exhibits antiproliferative activity against several cancer cell lines. However, metabolomic studies to evaluate the metabolite changes induced by E. indica in cancer cells are still lacking. The present study investigated the anticancer effects of a root fraction of E. indica (R-S5-C1-H1) on H1299, MCF-7, and SK-HEP-1 cell lines and analyzed metabolic changes in the treated cancer cells using ultra-high-performance liquid chromatography high-resolution mass spectrometry (UHPLC-HRMS). Cell metabolic activity assays demonstrated that the cell viability of the three cancer cell lines was significantly reduced following treatment with R-S5-C1-H1, with half-maximal inhibitory concentrations values of 12.95 μg/mL, 15.99 μg/mL, and 13.69 μg/mL at 72 h, respectively. Microscopy analysis using Hoechst 33342 and Annexin V fluorescent dyes revealed that cells treated with R-S5-C1-H1 underwent apoptotic cell death, while chemometric analysis suggested that apoptosis was triggered 48 h after treatment with R-S5-C1-H1. Deconvoluted cellular metabolomics revealed that hydrophobic metabolites were significantly altered, including triacylglycerols, phosphatidylcholine, phosphatidylethanolamine, sphingomyelin, and ceramide, suggesting that apoptosis induction by R-S5-C1-H1 potentially occurred through modulation of phospholipid synthesis and sphingolipid metabolism. These metabolomic profiling results provide new insights into the anticancer mechanisms of E. indica and facilitate the overall understanding of molecular events following therapeutic interventions.