Salvia pratensis exhibits in vitro anti-cancer effects in triple-negative breast cancer through *miR-34a-5p* signaling

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Introduction: Triple-negative breast cancer (TNBC) is the most aggressive malignancy in women, with limited treatment options and significant adverse effects. Natural products have emerged as promising anticancer agents, either alone or in combination with standard therapies. Within the National Biodiversity Future Center, this study aims to valorize Italy's plant biodiversity, as a source of novel bioactive compounds with therapeutic and nutraceutical potential.

Methods: Leaf extracts of *Petasites paradoxus*, *Salvia pratensis*, and *Typha laxmannii* were profiled by UPLC-ESI-HRMS. TNBC MDA-MB-231 and non-tumorigenic MCF 10A mammary epithelial cells were exposed to 5 µg/mL of each DMSO-resuspended extract. Viability, proliferation, migration, cell-cycle, and ROS were assessed. Genes and miRNA expression were quantified by RT-qPCR, supported by immunofluorescence, bioinformatic functional enrichment, and patients' survival analyses.

Results: Each species showed a specific phytochemical fingerprint. Notably, *S. pratensis*, enriched in rosmarinic acid, caffeic acid esters, and luteolin derivatives, selectively reduced TNBC cell viability after 24 hours. The treatment also impaired proliferation, migration, and cell cycle, increasing mitochondrial reactive oxygen species, and inducing apoptosis. Underlying the molecular mechanisms, *S. pratensis* stimulation modulated genes associated with tumor aggressiveness. Importantly, over-representation analysis on the differentially expressed genes pool identified miR-34a-5p as a potential regulator, its low expression being linked to poor TNBC prognosis. MiR-34a-5p in treated MDA-MB-231 was significantly up-regulated compared to controls.

Discussion: These findings position *S. pratensis* as a promising source of naturally derived bioactive compounds with selective anticancer activity, mediated in part via miR-34a-5p signaling. This study highlights the potential of plant-based bioactives for preventive and complementary strategies in TNBC, supporting further exploration of their integration into dietary or therapeutic interventions.