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Exploring plant metabolites to overcome multidrug resistance in cancer chemotherapy

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Cancer multidrug resistance (MDR) has been considered as one of the major obstacles for a successful chemotherapy. The most significant mechanism is due to the overexpression of transmembrane transporter proteins of the ATP-binding cassette (ABC) superfamily, which act as extrusion pumps for chemotherapeutic agents, decreasing their intracellular concentration. The most important ACB transporters associated with MDR are P-glycoprotein (P-gp), multidrug resistance protein (MRP1) and breast cancer resistance protein (BCRP). Aiming at obtaining plant-derived metabolites with improved MDR-reversing activity, we have evaluated as P-gp modulators a large number of natural compounds and derivatives, with different scaffolds, using both functional and chemosensitivity assays. Several compounds, namely alkaloid derivatives and nitrogen-containing flavonoids were also evaluated, using MRP1 and BCRP-overexpressing cancer cells as models. The anti-MDR potential of compounds was also assessed by evaluating their ability as collateral sensitivity agents, in resistant cancer cells [1-4].

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