Euryops pectinatus L. Flower Extract Inhibits P-glycoprotein and Reverses Multi-Drug Resistance in Cancer Cells: A Mechanistic Study

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Abstract

Euryops pectinatus is a South African ornamental plant belonging to family Asteraceae. The present work evaluates the cytotoxic activity and phytochemical profile of the flower extract. Metabolite profiling was performed using HPLC-PDA-ESI-MS/MS. Total phenolics and flavonoids content were assessed. Cytotoxicity was evaluated against 6 different cancer cell lines using MTT assay. The possible underlying mechanism was proposed. We analyzed whether the extract could overcome the resistance of multidrug-resistant cancer cells for doxorubicin. The effect of combination of E. pectinatus with doxorubicin was also studied. Additionally, the potential inhibitory activity of the identified phytochemicals to PB1 protein was analyzed using in silico molecular docking. Twenty-five compounds were tentatively identified. Total phenolic and flavonoid contents represented 49.41 Ñ 0.66 and 23.37 Ñ 0.23 Õg/mg dried flower extract, respectively. The extract showed selective cytotoxicity against Caco2 cells but its main effect goes beyond mere cytotoxicity. It showed strong inhibition of P-glycoprotein, which helps to overcome multidrug resistance to classical chemotherapeutic agents. In silico molecular docking showed that dicaffeoyl quinic acid, kaempferol-O-rutinoside, rutin, and isorhamnetin-O-rutinoside exhibited the most potent inhibitory activity to PB1 involved in tumor progression. Euryops pectinatus flower heads could have promising selective cytotoxicity alone or in combination with other chemotherapeutic agents to counteract multidrug resistance.

Molecules 2020, February