

## **Evaluation of protective effect against H<sub>2</sub>O<sub>2</sub>-induced oxidative stress and cytotoxic activity of a phenolic-rich fraction obtained from the leaves of *Isatis tinctoria* L. (Brassicaceae)**

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*Isatis tinctoria* L. (woad) is a herbaceous biennial species belonging to Brassicaceae, traditionally used for the treatment of wounds, ulcers, haemorrhoids, tumours and inflammatory diseases. Several studies demonstrated the anti-inflammatory and anti-cancer properties of lipophilic extracts and isolated compounds from the leaves of *I. tinctoria*, whereas few studies have been carried out to determine the biological properties of polar constituents present in this species.

Aim of the present study has been the evaluation of some biological activities of the phenolic-rich fraction (ItJ-EAF), phytochemically characterized, obtained from cauline leaves picked in January from *I. tinctoria*. In particular, the protective effect against H<sub>2</sub>O<sub>2</sub>-induced oxidative stress and the cytotoxic activity were investigated.

The phenolic profile of ItJ-EAF was investigated by HPLC-PDA-ESI-MS analysis: flavonoids (flavones and flavonols) and cinnamic acids were identified. Flavone glycosides were quantitatively the most abundant constituents, and vicianin-2 resulted the main flavonoid. In order to establish the antioxidant efficacy of ItJ-EAF in a complex biological setting, the protective ability on *Escherichia coli* ATCC 25922 subjected to oxidative stress damage caused by H<sub>2</sub>O<sub>2</sub> was investigated. In this in vivo experimental model, the fraction didn't show any effect. The anti-proliferative effect of ItJ-EAF on two human thyroid carcinoma cell lines (CAL-62 and 8505C) was evaluated by MTT assay. The fraction reduced the proliferation of both cell lines with similar trend. The strongest effect was observed in CAL-62 cells; particularly, after 48 h exposure, ItJ-EAF markedly inhibited cell growth at the concentration of 0.05 mg/mL (approximately 50% vs untreated cells,  $p < 0.01$ ) and at 0.1 mg/mL (approximately 80% vs untreated cells,  $p < 0.001$ ). Minor but significant effect was found in 8505C cells: after 48 h of treatment, about 45% at the concentration of 0.05 mg/mL and 65 % with 0.1 mg/mL of fraction was found ( $p < 0.01$  vs untreated cells). The effects of ItJ-EAF are comparable or even stronger than those of Sunitinib, a protein kinase inhibitor used in the treatment of thyroid cancer.

These results demonstrated that *I. tinctoria* cauline leaves represent a source of phenolic compounds which could be potentially used as chemopreventive or adjuvant agents against cancer.