

Alcoholic extracts of *Epilobium*, *Urtica dioica* and *Evernia prunastri* with 5-fluorouracil in controlling murine colon carcinoma cell growth in vitro

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Abstract In recent years, there has been growing interest in plant-derived products for their bioactive properties. Results and Conclusion. This study aimed to verify the effect of an herbal-food supplement, comprising alcoholic extracts of *Epilobium*, *Urtica dioica* and *Evernia prunastri* (YATROS, Etnopharma, Turin, Italy), alone or in combination with 5-Fluorouracil, on cell growth, DNA synthesis, cell-cycle profile, cytoskeleton reorganization and E-cadherin protein expression, in the murine colon carcinoma cell line C26. Assays used were respectively the Neutral Red uptake assay, median effect analysis, tritiated thymidine incorporation, flow cytometry, Phalloidin staining, and immunohistochemistry. A chemical fingerprint and multidimensional HPLC-UV-HRMS analysis was also performed on the herbal-food supplements. Intriguingly, a substantial synergistic inhibitory effects on cell growth, DNA synthetic activity and percentage of cells in S phase were noticed when YATROS was combined with 5-Fluorouracil, reducing both dose and timing of exposure of C26 cells to the drug. Moreover, by inducing cytoskeleton reorganization and E-cadherin expression, YATROS can interfere with tumor cell invasiveness. These indications of an

agonistic interaction between YATROS and 5-Fluorouracil in colon carcinoma cells may be of interest for clinical applications, and thus merit further investigation.

Keywords *Epilobium* · *Urtica dioica* · *Evernia prunastri* · Herbal-food supplement · Colorectal carcinoma · 5-fluorouracil

Introduction

There is renewed global interest in herbal medicines in the area of disease management, as their clinical efficacy and mechanisms of action are being elucidated. Considerable progress has been made, with scientific reports on physiological and cellular effects of herbals as immunomodulatory, antitumor, antimicrobial and antioxidative agents.

YATROS (Etnopharma, Turin, Italy) is a herbal-food supplement comprising alcoholic extracts of several medical plant species, known to possess many therapeutic properties. In particular, it contains three different species of *Epilobium* (*Epilobium parviflorum*, *Epilobium angustifolium*, *Epilobium hirsutum*), together with *Urtica dioica* and *Evernia prunastri*.

Epilobium species are rich in macrocyclic tannins, flavonoids, phytosterols and polyphenols (Ducrey et al. 1995; Hierman 1995), traditionally used to treat a variety of medical problems, such as gastrointestinal, and prostate diseases, and to improve the healing of wounds (Vitalone et al. 2003; Safarinejad 2005; Hevesi Tóth et al. 2009; Shoskes and Manickam 2003; Steenkamp et al. 2006).

Oenothien B, a dimeric macrocyclic ellagitannin, the major component of *Epilobium* species (Ducrey et al. 1997), has been reported to exhibit significant immunomodulatory,

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