

# **IN VITRO GENOTOXICITY TESTING OF BOTANICAL MATRIXES DERIVED FROM *Foeniculum vulgare* (FENNEL)**

Sara Levorato<sup>1,3</sup>, Samuele Vannini<sup>1</sup>, Rita Pagiotti<sup>2</sup>, Luca Dominici<sup>1</sup>, Cristina Fatigoni<sup>1</sup>, Massimo Moretti<sup>1</sup>, Milena Villarini<sup>1,®</sup>

<sup>1</sup>Dept. of Medical-Surgical Specialties and Public Health (Section of Public Health), University of Perugia, Via del Giochetto, 06122 Perugia, Italy. <sup>b</sup>Dept. of Applied Biology (Section of Plant Biology and Geobotany), University of Perugia, Borgo XX Giugno, 06121 Perugia, Italy. <sup>3</sup>School of Advanced Studies (Area: Life Sciences and Public Health; Ageing and Nutrition), University of Camerino, Via Gentile III da Varano, 62032 Camerino, Italy. <sup>®</sup> milena.villarini@unipg.it.

**Background** - *Foeniculum vulgare* Mill. (fennel), a perennial herb with a characteristic aniseed flavour, belongs to the Apiaceae (Umbelliferae) family, being native to the circum-Mediterranean area, yet naturalized in northern Europe, Australia and North America and cultivated worldwide. A number of beneficial properties have been attributed to fennel fruits. Among the best characterized are anti-inflammatory, analgesic, antibacterial, and antioxidant properties. Fennel infusion, with a mild flavor and good tolerance, is currently regarded as a first-choice treatment in infants and sucklings with dyspeptic disorders. However, estragole, present in this herbal remedy, has been reported to produce hepatic tumors in susceptible strains of mice and a Scientific Committee on Food of the European Commission recommended restrictions in use of estragole-containing remedies.

**Methods** - The present study was undertaken to evaluate, in the human hepatoma cell line HepG2, the *in vitro* cytotoxic, genotoxic and apoptotic activities of three botanical matrixes derived from *Foeniculum vulgare* Mill. (fennel): (i) fennel seed lyophilised extract (FSLE), (ii) very fine fennel seed powder (VFFSP), and (iii) fennel seed essential oil (FSEO). Estragole was tested as well. To this purpose, the MTT cytotoxicity assay, the trypan blue dye exclusion test, the double staining (acridine orange and DAPI) fluorescence viability assay, the single-cell microgel-electrophoresis (comet) assay, the mitochondrial membrane potential ( $\Delta\psi_m$ ) assay and the DNA fragmentation analysis were used. To the best of our knowledge this is the first research aimed at examining the toxicity of naturally multicomponent mixtures (such as FSLE, VFFSP, FSEO) in human cells, as compared to the purified form of the putative toxicant.

**Results** - As regards genotoxic effects, the comet assay indicated that the compounds tested were not able to induce DNA damage under conditions used in our experiments. FSLE, VFFSP and estragole did not induce apoptosis. Whereas, HepG2 cells treated with FSEO exhibited a marked increase in early and late apoptosis.

**Discussion** - Our results demonstrate that FSLE, VFFSP and estragole are not cytotoxic, genotoxic and apoptotic in HepG2 cells line. On the basis of these findings we think our data can confirm that fennel decoction (and the exposure to estragole resulting from consumption of food) does not rise significantly the risk of primary liver cancer. Moreover data from this *in vitro* study suggested for FSEO apoptotic (antitumor ?) actions against malignant HepG2 cells. However, prospective cancer-suppressive effects of the tested essential oil should be further evaluated in *in vivo* experiments.

## **References:**

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