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Ferutinin: A Natural and Effective anti-tumour Compound

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ABSTRACT

In spite of major advances in cancer chemotherapy, effective response is obtained only in a small proportion of patients, which is due to acquired drug resistance of cancer cells. *Ferula* species are good sources of sesquiterpenes, which are *naturally occurring hydrocarbons* with antimicrobial, antiviral, anticancer, anti-malarial and anti-inflammatory activities. Ferutinin, is a sesquiterpene *found* in umbelliferae family which has shown antimycobacterial, anti-inflammatory, antifungal, and apoptosis inducing activities. In present study, ferutinin was isolated from the roots of *Ferula ovina* and evaluated for its possible cytotoxic effects on human NTERA2 (human teratocarcinoma) and KYSE30 (esophageal cancer) cell lines. To determine IC_{50} values of this compound NTERA2 and KYSE30 cells were treated with different concentrations of ferutinin (5-100 µg/ml). After 24, 48 and 72 h cell viability was quantified by MTT assay and morphological changes were observed under a microscope. In order to study its mechanism of action, DNA damage was detected using DAPI staining on KYSE30 cells. Analysis of cell survival by MTT assay showed that the IC_{50} of ferutinin on NTERA2 cells were 17, 14 and 13 µg/ml after 24, 48 and 72 h of its administration, respectively. Moreover, the IC_{50} values were calculated as 22, 21 and 14 µg/ml on KYSE30 cells after 24, 48 and 72 h of treatment. The microscopic observations also revealed that the morphology of cells was changed to spherical forms with granulated cytoplasm in comparison to controls. DAPI staining revealed that ferutinin significantly induced DNA damage in treated cells. In previous studies, we demonstrated that ferutinin induces apoptosis in human TCC (transitional cell carcinoma), MCF7 (breast cancer), HT29 and CT26 (human and mouse colon carcinoma) cell lines. In addition, our recent *in vitro* results showed that this compound was more efficient than vincristine and doxorubicin, routine anticancer drugs. Furthermore, our *in vivo* data revealed that ferutinin, similar to cisplatin, reduced tumour growth in a mouse colon tumour model as compared to control groups and no significant toxicity was observed in vital organs like spleen and liver. Here, anticancer effects of ferutinin were demonstrated on other types of cancers; i.e. human teratocarcinoma and esophageal cancer cell lines. Thus, this sesquiterpene could be considered as a natural and effective anticancer agent for future preclinical studies.

Key words: *Ferula ovina*, Sesquiterpene, Ferutinin, Cytotoxicity, Apoptosis

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