

Ethnopharmacology & Physiotherapy Congress 2019: Biological effects of ef24, a curcumin derivative, alone or combined with mitotane in adrenocortical tumor cell lines - Raffaele Pezzani - University of Padova

Raffaele Pezzani

University of Padova, Italy

Background: Curcumin is a polyphenol extracted from the plant *Curcuma longa* L. It has numerous properties and is used in many preclinical conditions, including cancer. Curcumin has been tested in colorectal, lung, breast, liver and many others tumor cell lines. It is known that curcumin has low bioavailability, while its derivative EF24 showed enhanced solubility. However, its effects have been never explored in adrenocortical tumor cell models. Adrenocortical tumors (ACT) are common diseases with a prevalence of 3–10% in the general population and can be categorized into adrenocortical adenomas (ACA), which is more frequent, and adrenocortical carcinoma (ACC), which is very rare and has an incidence of 1 to 2 per million per year. ACC has a five-year survival rate of approximately 20–35% and can frequently metastasize; for these reasons, the prognosis is often poor. Moreover, the majority of patients are diagnosed with advanced disease, which does not permit an actual ACC treatment. However ACC management is essentially based on surgical removal of the mass, which is the only complete curative option. When at the diagnosis, a metastasis is detected, clinicians can use mitotane, the reference adrenotoxic agent approved for ACC, in addition to cytotoxic drugs that should be supplemented in case of disease progression.

Aim: This work analyzed the efficacy of EF24, a curcumin derivative, in 2 adrenocortical tumor cell line models, SW13 and H295R.

Results: EF24 reduced cell viability by MTT with IC₅₀ of 6.5 ± 2.4 μ M and 4.9 ± 2.8 μ M for SW13 and H295R cells, respectively. Combination index (EF24 associated with mitotane) suggested an additivity effect in both cell lines. Cell cycle analysis revealed an increase of subG₀/G₁ phase, while motility assay showed a decrease in migratory cell capacity after drug treatment and similarly clonogenic assay indicated that EF24 (alone or combined with mitotane) could reduce colonies number. Also, Wnt/ β -catenin, NF- κ B, MAPK and PI3k/Akt pathways were modulated by western blot analysis when treating cells with EF24 alone or combined with mitotane.

Conclusions: This work analyzed for the first time a derivative of curcumin, EF24, in adrenocortical tumor cell lines. These results suggest that EF24 could potentially impact on

adrenocortical tumors, laying the foundation for further research.