Anticancer effects of Olive Leaf Extract (OLE) on lung cell lines A549 and MRC5 and its possible modulating effect on cisplatin toxicity

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Natural polyphenols are well-known for their healthy effects. Olive leaf extract (OLE) contains much more and different types of polyphenols than those found in extra virgin olive oil, which is the basis of traditional Mediterranean diet. The most abundant polyphenol in OLE is oleuropein, which plays an important protective role in cancer cell models, due to both anti- inflammatory properties and protection against DNA damage produced by free radicals of oxidative stress.

Cisplatin is a routine chemotherapeutic drug used against solid tumors with toxic side effects. This crosslinker agent may insert into the purine bases on the DNA, interfering with DNA repair mechanisms, causing DNA damage and apoptosis in cancer cells. Platinum based drugs are often used as standard treatment in lung cancer. Their non-specificity is a major challenge because these compounds not only kill cancer cells but also are extremely toxic for normal cells.

In this work we have studied the possible antitumor activity of OLE extract, either alone or in combination with cisplatin, on a human lung carcinoma *in vitro* model. For that, we used the A549 lung adenocarcinoma cell line and the MRC5 normal cell line. Cell viability was measured by sulphorhodamine assay, DNA damage was analyzed by γ-H2AX foci assay, and cell cycle progression was assessed by flow cytometry.

Our results reflect a great decrease in cell viability in A549 cancer cells and MRC5 normal cells exposed to OLE extract and cisplatin alone. The treatment with OLE and cisplatin together decreases the cell viability of A549 cancer cell line too. What is more, this combination of drugs produces a remarkable protective effect in MRC5 normal cells, comparing with these drugs alone. These results indicate that the combined treatment could be more selective preventing the damage in normal cells than the usual therapy only with cisplatin in lung carcinoma. The oleuropein may be responsible of this protective effect. Regarding the non-specificity and the side effects of the cisplatin treatment in human lung cancer, the addition of OLE extract could improve the protection of normal cells resulting in a less harmful chemotherapy.

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