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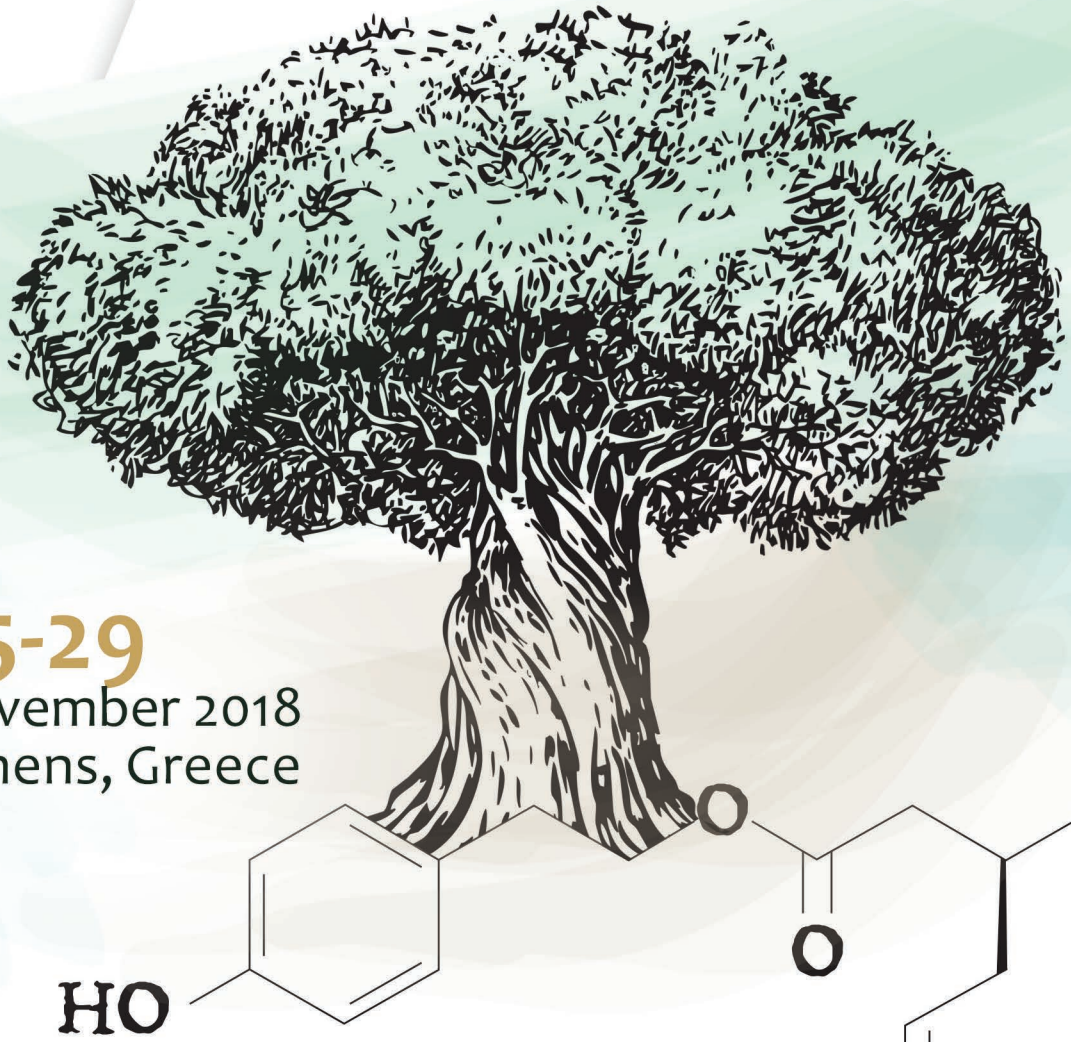

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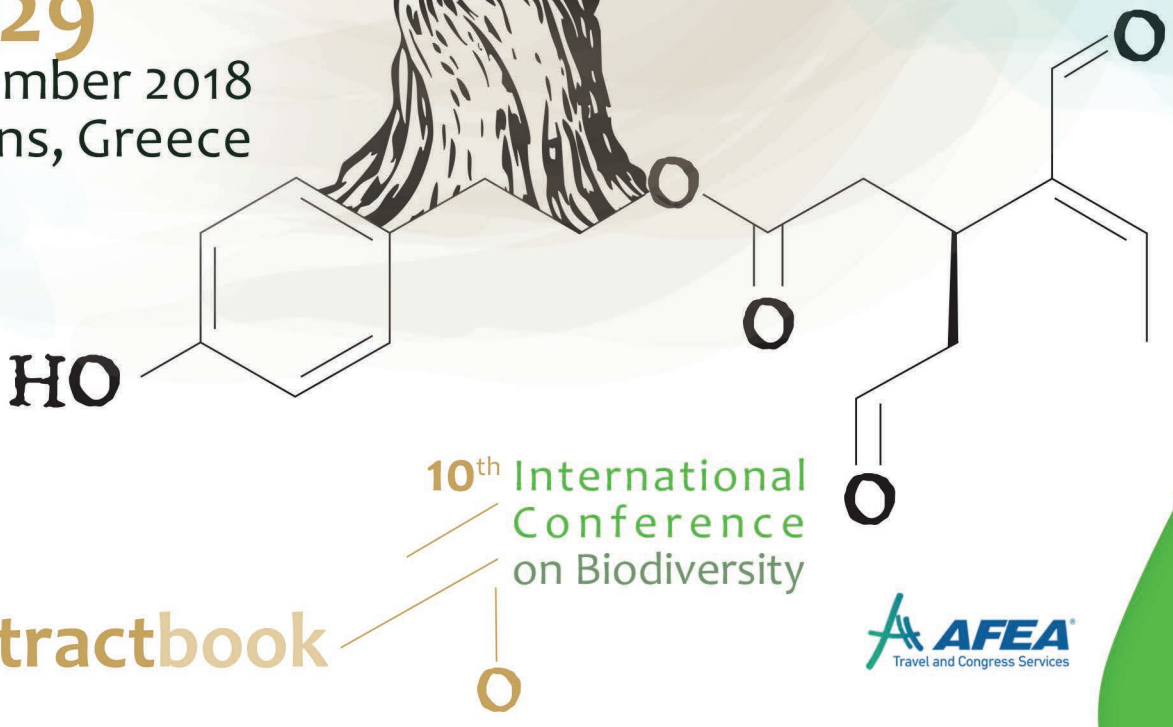

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abstractbook

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A natural oxadiazine isolated from cyanobacteria kills cancer cells in multicellular culture systems by impairing cellular respiration

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Cyanobacteria are versatile microorganisms that ubiquitously inhabit terrestrial and aquatic ecosystems. They adapt to external threats by mainly producing secondary metabolites. Therefore, cyanobacteria have been recognized as producer of natural products with potential biotechnological applications, such as bioplastics, antifouling, antibiotics, antiprotozoal or anticancer treatment.

A known compound with an oxadiazine ring (Nocuolin A) was re-isolated from the cyanobacteria strain *Nodularia* sp. LEGE06071. These heterocyclic rings were already reported as having anticancer properties, namely as telomerase inhibitors, kinase inhibitors, among others. Nocuolin A (NocA) was demonstrated to be cytotoxic against various cancer cell lines, inducing apoptosis.

In the present study, the activity of NocA was analysed on colon carcinoma cells (HCT116) cultured as monolayer or as multicellular culture systems (MTS). Cancer cells within a tumour are hypoxic and nutrient-deprived, and so, commonly chemotherapy treatments fail to treat the inner part of tumours. 3D cultures of cancer cells represent a good model *in vitro* with high physiological relevance.

In monolayer culture, ATP production was decreased after 2 h of exposure in a dose-dependent manner. After analysing cellular respiration rates over 6 h, oxygen consumption was significantly decreased, indicating an impairment of mitochondrial respiration. Moreover, non-mitochondrial respiration rates were also reduced, indicating that both respiration mechanisms are damaged.

In MTS, exposure to NocA induced apoptosis analysed by the M30 Apoptosense assay. Analysis by fluorescence microscopy of MTS stained with Propidium Iodide also confirmed the tumour cell death, and activity of NocA in 3D cultured colon cancer cells.

The imbalance of ATP caused by NocA makes it an interesting candidate to further study its effects on hypoxic cores of tumours.

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References:

[1] PLOS One 2017, 12(3): e0172850