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Essential oil of *Citrus lumia* risso: Phytochemical profile, antioxidant properties and activity on the central nervous system

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Background: The use of essential oils (EOs) is known since long time in traditional medicine and aromatherapy for the management of various oxidative stress-related disorders and is further increased recently for their neuroprotective and anti-aging potential as well as for reducing anxiety and stress.

Purpose: To evaluate, for the first time, the chemical composition of *Citrus lumia* Risso EO and its antioxidant, anti-cholinesterase as well as neuroactive properties by cell-free and cell-based assays. *Citrus lumia* Risso is one of the oldest cultivated limettes in Sicily, Mediterranean Europe and North Africa by which distinguished for the fruit shape and mainly for the sweet, no-acidic juice.

Methods: The distribution and morphology of oil glands in the fruit peel were analysed microscopically, by SEM. A phytochemical profile elucidation, by GC-FID and GC-MS analysis, an *in vitro* evaluation of antioxidant and free-radical scavenging properties of the EO, using different *in vitro* methods (Folin-ciocalteu, DPPH, TEAC, FRAP, Fe^{2+}-chelating capacity, ORAC and β-carotene bleaching assays) as well as anti-cholinesterase activity were carried out. The impact on the spontaneous electrical activity of rat neuronal networks by means of microelectrode array (MEA)-based system, was evaluated.

Results: The EO has shown strong antioxidant and free radical scavenging properties, particularly in hydrogen atom transfer based assays (β-carotene bleaching and ORAC assay, IC_{50} 22 μg/mL and 46 μg/mL, respectively), that can be attributed to the high content of monoterpene and monoterpene derivatives, especially d-limonene (48.905%), and linalool (18.245%). Furthermore, has shown an interesting anti-acetylcholinesterase activity (IC50 258.25 μg/mL). Data from MTT analysis indicate that the cytotoxicity of OE, evaluated on L929 mouse fibroblasts, is very low, with an IC50 higher than 500 ug/mL at 48 h. Rat neuronal networks subjected to EO showed a concentration-dependent inhibition of spontaneous electrical activity.

Conclusions: Results indicate that this EO could be an important source of natural antioxidants potentially useful in the detoxification mechanisms of the organism, suggesting an important preventive role in the onset of oxidative stress-related pathologies.

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