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In vitro neuronal characterization of the entheogenic plant *Tagetes lucida* Cav.

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Abstract

Background: Holding a relevant ritualistic and ethnomedicinal value among the Mesoamerican tribes, *Tagetes lucida* Cav. has recently seen its uses being translated into Western communities, primarily for recreational ends, given its psychoactivity. Despite the new popularity resurgence of entheogens, the available data concerning this plant's pharmacological and safety profile remain scarce [1-3]. **Objective:** This study aimed to elucidate the bioactive compounds found in *T. lucida* aerial parts and assess their neuropharmacological and toxicological properties. **Methods:** Chemical characterization was performed by means of chromatographic hyphenated techniques. Cytotoxic potential was assessed using human neuroblastoma SH-SY5Y cells, through the evaluation of the mitochondrial and lysosomal performance, and cellular integrity [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, mitochondrial membrane potential, neutral red, and lactate dehydrogenase (LDH) assays; up to 1000 µg mL^{-1}]. Neuronal excitotoxic potential was also explored, following a direct glutamate stimulus, while the inhibition of acetylcholinesterase (AChE) and monoamine oxidase A (MAO-A) was attained in a cell-free model to assess neuromodulatory effects. **Results:** Within the aqueous extract of the aerial parts, the majority of the detected secondary metabolites corresponded to phenolic acid derivatives, followed by coumarins and flavonoids, with scoparone and herniarin being identified as the main compounds. While lysosomal integrity was preserved under normal conditions, mitochondrial depolarization was noted from 250 µg mL^{-1} onwards, while impairment of metabolic competence and loss of membrane integrity with LDH release were verified at the highest tested concentration. When co-exposed to glutamate, neuroprotection was observed from 62.5 to 250 µg mL^{-1}, counteracting its excitotoxic effects. Additionally, concentration-dependent neuromodulation was achieved via AChE and MAO-A inhibition, starting at 31.25 and 15.625 µg mL^{-1}, respectively. **Conclusions:** Considering the neurotoxic effects, indicated by loss of cell metabolic competence and integrity, and the neuroprotective potential, upon glutamate exacerbation, our findings highlight the paradoxical effects promoted by *T. lucida*. Moreover, the inhibition of both neurotransmitter-degrading enzymes suggests apparent pharmacological properties. Nonetheless, these results call for further investigation to unravel the underlying mechanisms.

Keywords: oneirogenic; recreative settings; excitotoxicity; Mexican tarragon; ethnomedicine

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