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Chemical characterization and in vitro studies on the impact of the 'Dream Herb' *Calea zacatechichi* Schltdl. upon neuronal cells

Maria Rita Garcia [1,2,3,4,5,*], Tiago Mineiro [1,2], Paula B. Andrade [3], Federico Ferreres [6], Ángel Gil-Izquierdo [7], Vítor Seabra [1,2], Diana Dias-da-Silva [1,2,3,4,5,8] and Nelson G. M. Gomes [3]

[1] Associate Laboratory i4HB – Institute for Health and Bioeconomy, University Institute of Health Sciences – CESPU, 4585-116 Gandra, Portugal
[2] UCIBIO – Applied Molecular Biosciences Unit, Forensics and Biomedical Sciences Research Laboratory, University Institute of Health Sciences (1H-TOXRUN, IUCS-CESPU), 4585-116 Gandra, Portugal
[3] REQUIMTE/LAQV, Laboratório de Farmacognosia, Departamento de Química, Faculdade de Farmácia, Universidade do Porto, Porto, Portugal
[4] UCIBIO/REQUIMTE, Laboratory of Toxicology, Faculty of Pharmacy, University of Porto, Porto, Portugal
[5] Associate Laboratory i4HB - Institute for Health and Bioeconomy, Faculty of Pharmacy, University of Porto, Porto, Portugal
[6] Department of Food Technology and Nutrition, Molecular Recognition and Encapsulation (REM) Group, Universidad Católica de Murcia, Murcia, Spain
[7] Research Group on Quality, Safety and Bioactivity of Plant Foods, CEBAS (CSIC), Murcia, Spain
[8] LAQV/REQUIMTE, ESS, Polytechnic of Porto, Rua Dr. António Bernardino de Almeida, 400 4200 - 072, Porto, Portugal

* Correspondence: ritagarcia7@hotmail.com

Abstract

Background: An increasing number of psychoactive plants, particularly those with long history of use on ritualistic practices, are now being progressively used in recreational context, many of which remaining unregulated [1]. *Calea zacatechichi* is traditionally used in divination rituals, due to its oneirogenic properties. Yet, considering the psychoactive effects of this 'Dream Herb' and easiness of purchase, the potential for recreational use is high, with scarce information concerning its toxicity [2-4]. **Objective:** We aimed to characterize *C. zacatechichi* aqueous extracts, mimicking those typically consumed, to identify bioactives that underlie the psychoactive or toxic effects, and evaluate their impact upon neuronal function, neurotransmission and radical stress. **Methods:** Chemical characterization was attained by HPLC-DAD-ESI (Ion Trap)/MS^n and HPLC-DAD. Impact upon SH-SY5Y and BV-2 cell viability was assessed by the MTT assay and LDH release (up to 1000 µg/mL). Impact on neuromodulation and neuroinflammation was evaluated through acetylcholinesterase and 5-lipoxygenase inhibition, while antiradical properties were approached upon nitric oxide ($^{\bullet}NO$) and superoxide ($O_2^{\bullet-}$). Statistical comparisons among groups performed by one-way ANOVA followed by Dunnett post hoc test. **Results:** Qualitative analyses enabled the identification of 28 compounds, the majority being hydroxycinnamic acid derivates, namely 3,5-dicaffeoylquinic acid and 4,5-dicaffeoylquinic acid, followed by flavonoid derivates, particularly quercetin-3-*O*-rutinoside. Cytotoxic effects were verified at concentrations above 125 µg/mL with LDH leakage starting at 250 µg/mL. Acetylcholinesterase inhibition was recorded at 1000 µg/mL, and a concentration-dependent inhibition of 5-lipoxygenase was found (IC_{50} = 71.12 µg/mL). Concentration-dependent scavenging effects upon $^{\bullet}NO$ and $O_2^{\bullet-}$ were verified at concentrations higher than 62.5 µg/mL. **Conclusions:** Even though apparent antiradical and anti-inflammatory properties were attained with *C. zacatechichi*, the pronounced cytotoxic effects upon neuronal cells cannot be overlooked, requiring further investigation to elucidate the underlying mechanisms that might be involved, given the possible deleterious consequences this plant can induce among its consumers.

Keywords: new psychoactive substances; oneirogenic plants; recreational setting; phytochemical characterization; neurotoxicity

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References

1. European Monitoring Centre for Drugs and Drug Addiction, European Drug Report 2022: Trends and Developments, Publications Office of the European Union (2022).
2. Mata R et al. Calea ternifolia Kunth, the Mexican “dream herb”, a concise review. Botany. (2022) 100, 261–74;
3. Leonti M et al. Antiquity of medicinal plant usage in two Macro-Mayan ethnic groups (México). J Ethnopharmacol. (2003) 88, 119–24;
4. Martinez-Mota L et al. Calea zacatechichi Schltdl. (Compositae) produces anxiolytic- and antidepressant-like effects, and increases the hippocampal activity during REM sleep in rodents. J Ethnopharmacol. (2021) 265.