

# **In Vitro Toxicological and Anti-inflammatory Effects of The Phytochemical Marker Coumarin from Mikania sp. (Guaco): A Systematic Review and Cytotoxicity in J774A.1 Macrophage Cell Line**

**Beatriz Scaramelo**<sup>1</sup>; Yasmin C. G. da Silva<sup>1</sup>; Fabio Coelho Amendoeira<sup>1</sup>; Caio Eduardo L. Gomes<sup>1</sup>; Izabela Gimenes Lopes<sup>1</sup>; Fausto Klabund Ferraris<sup>1</sup>

<sup>1</sup>Laboratório de Farmacologia, Instituto Nacional de Controle de Qualidade em Saúde – FIOCRUZ, Rio de Janeiro, Brasil.

**INTRODUCTION:** The two species of *Mikania* (*M. glomerata* and *M. levigata*), commonly called "guaco" in Brazil, are used in traditional Brazilian medicine to treat diseases such as asthma, bronchitis, relieve coughs and aid in the healing of wounds and eczema. The Brazilian Pharmacopoeia of Phytotherapeutics determines the analysis of coumarin content as the phytochemical marker linked to the quality control of Guaco and its derived products. **OBJECTIVE:** The aim of this study was to summarize the current evidence on the anti-inflammatory and toxic activity of coumarin in the literature, evaluating the association between therapeutic concentrations and toxicity threshold. Based on the concentrations found, the toxicity of coumarin was evaluated in vitro. **MATERIAL AND METHODS:** The systematic review followed the PRISMA 2020 guideline. An electronic search was performed in three databases and grey literature. Studies that conducted *in vitro* techniques exposed to coumarin, and that reported an assessment of toxicological or anti-inflammatory effects were included. The methodological quality was assessed using the ToxRTool. For cytotoxicity evaluation, cells from the murine macrophage cell line J774A.1 were cultured in 96-well microplates and incubated with coumarin at concentrations of 1, 10, 50, 100, 200 and 300 µg/mL for 24 hours. Viability was assessed using the MTT method. **RESULTS:** From 396 identified studies, 4 were included according to the eligibility criteria. All studies were considered "reliable without restriction" due to good methodological quality. RAW 264.7 cell line was the most used model. MTT was the most common method to assess cell viability, within a concentration range of 0-500 µg/mL. Two articles determined the anti-inflammatory activity of coumarin through the Nitric Oxide and TNF-  $\alpha$ , in addition to IL-6, IL-1 $\beta$ , and PGE2. In the in vitro evaluation, coumarin reduced cell viability by 72%, 50%, and 45% when exposed at concentrations of 100, 200, and 300 µg/mL, respectively. **CONCLUSION:** Comprehensive *in vitro* investigations of coumarin are essential for elucidating the pharmacological mechanisms and ensuring the safety of this phytochemical marker. Such studies may significantly contribute to the enhancement of quality control measures for herbal medicines derived from the *Mikania* (guaco) species.

**Palavras-chave:** Toxicity Tests; Phytotherapy; traditional medicine.

**Apoio Financeiro:** Inova FIOCRUZ