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DISCRIMINATING ANTI-INFLAMMATORY COMPONENTS OF LYCHNOPHORINAE SPECIES (ASTERACEAE) BY UNTARGETED METABOLOMICS AND *IN SILICO* CORRELATION ANALYSIS

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Several compounds from Lychnophorinae species (Asteraceae) are reported as inhibitors of cascade mediators that elicits the inflammatory process. During this process, two enzymes are essential in the metabolism of the arachidonic acid: cyclooxygenase (COX) and lipoxygenase (LOX). Metabolomics comprises analytical methodologies that undergo a metabolic fingerprint containing full information of the object in the study, thus enabling to determinate differences among biological samples using statistical tools, and to correlate the obtained data through *in silico* methods. This work therefore aimed to analyze the anti-inflammatory potential of 21 species of the Lychnophorinae subtribe through *in vitro* inhibition of COX and LOX, to obtain metabolite fingerprinting data and to identify bioactive compounds by *in silico* correlation analysis. The metabolomic analysis was carried out using UHPLC-DAD-ESI-Orbitrap and a metabolic fingerprint for each extract was obtained. The *in vitro* inhibition screening assays of COX and LOX revealed that 16 extracts presented simultaneous inhibitory activity on both enzymes with IC_{50} values lower than 100 µM. Of these, nine species showed IC_{50} values lower than 40 µM and three lower than 10 µM. Supervised multivariate statistical analysis was performed using the software SIMCA-P (Umetrics). The results showed good separation of classes and high multiple correlation coefficients (R^2Y) both in the analysis by Partial Least Squares (PLS, R^2Y 0.996) and Orthogonal PLS (OPLS, R^2Y 0.993). Through correlation analysis, it was possible to locate the chromatographic peaks most likely to be responsible for the pharmacological activity in both enzymes simultaneously; among them, six were chosen as the most likely. Three of them were identified by dereplication and belong to the flavonoids, sesquiterpene lactones and sesquiterpenes classes. In summary, in this work it was possible to reveal crude extracts with outstanding anti-inflammatory potential by inhibition of both COX and LOX enzymes as well as to propose the most probable compounds responsible for this action. Therefore, species of Lychnophorinae show great anti-inflammatory potential and flavonoids and sesquiterpene lactones could be proposed as good COX and LOX inhibitors. In order to confirm our hypothesis, the next step is to identify the other discriminant compounds, isolate the proposed active compounds and test them directly on the enzymes.

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