Metabolite profiling of sesquiterpene lactones and phenolics of bioactive extracts from Asteraceae medicinal plants by HPLC-UV-MS

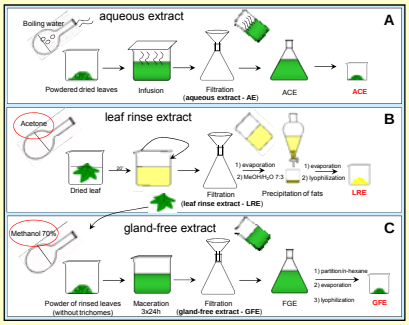
Gobbo-Neto, L; Silva, VC; Passoni, FD; Chagas-Paula, DA; Oliveira, RB; Da Costa, FB *e-mail: gobbo@fcfrp.usp.br*

University of São Paulo (USP), Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Av. do Café s/no., 14040-903, Ribeirão Preto, SP, Brazil

Introduction: *Tithonia diversifolia* (Hemsl.) A. Gray and *Smallanthus sonchifolius* (Poepp. e Endl.) H. Robinson (Asteraceae) leaves' infusions are used in folk medicine as anti-inflammatory. Both species possess glandular trichomes on their foliar surfaces where sesquiterpene lactones (STLs) are stored. STLs comprise a class of secondary metabolites to which at least part of the anti-inflammatory activity of Asteraceae species has been attributed. Furthermore, STLs are also related to several cases of Asteraceae species' toxicity.

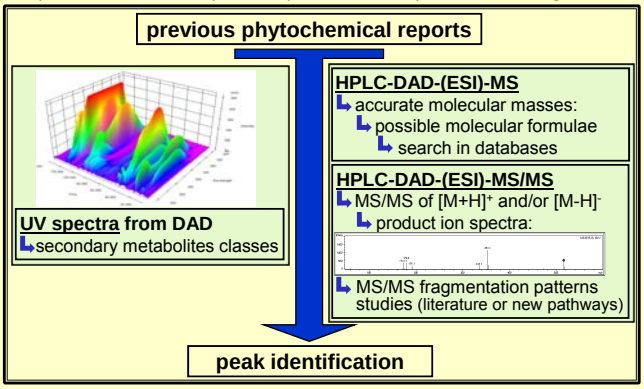
Aims: To compare the chemical composition of different extracts of *S. sonchifolius* (yacón) and *T. diversifolia* (Mexican sunflower) and correlate their metabolic profilings to anti-inflammatory and toxic effects.

Experimental: Different extracts were obtained from leaves from each plant species (**Scheme 1**):



Scheme 1. Preparation of different extracts of *S. sonchifolius* (yacón) and *T. diversifolia* (Mexican sunflower): aqueous crude extract (ACE), grand-free extract (GFE) and leaf rinse extract (LRE).

Metabolic profiling and dereplication have been performed by HPLC-UV(DAD)-MS(ESI-QqTOF) using a C18 monolithic column (200 *x* 3mm), 0 a 45% MeCN (1%HAc) over 45min (**Scheme 2**, **Figs. 1** and **2**).



Scheme 2. Chromatographic peaks identification using UV and MS data.

The toxic effects as well as anti-inflammatory properties were evaluated *in vivo* (rat paw and croton oil ear oedema assays) and *in vitro* (MPO, IL-10 and TNF-α).

Results:

More than different 50 compounds in the metabolic profilings were identified (**Figs. 1** and **2**). Both LREs were composed mainly of STLs and flavonoids. The major peaks in *T. diversifolia* LRE were the STL tagitinin C and the flavone hispidulin. The major peaks in *S. sonchifolius* LRE were the STLs enhydrin and uvedalin, along with minor structurally-related STLs, as well as the flavonoid isoquercitrin. GFE and ACE from both plants were constituted mainly by caffeic acid derivatives (chlorogenic acids in *T. diversifolia* and caffeoylaltraric acids in *S. sonchifolius*). STLs were not detected in both GFE, while in ACEs traces of STLs were detected. All extracts presented anti-inflammatory potential (**Fig. 3**) but the LREs were found to be highly toxic while the GFEs basically did not present significant toxicity **(Scheme 3**).

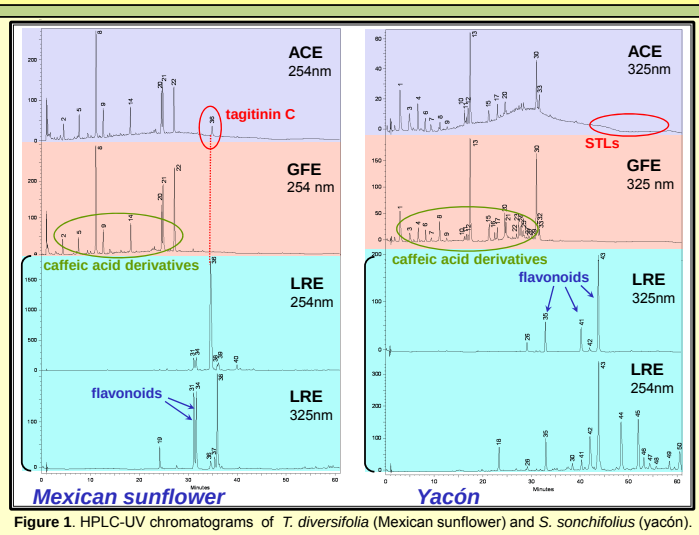


Figure 1. HPLC-UV chromatograms of *T. diversifolia* (Mexican sunflower) and *S. sonchifolius* (yacón).

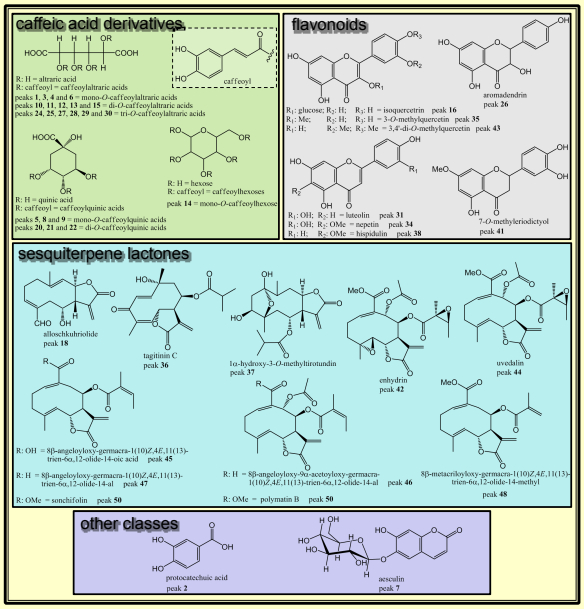


Figure 2. Compounds identified in metabolite profilings of *T. diversifolia* and *S. sonchifolius* extracts.

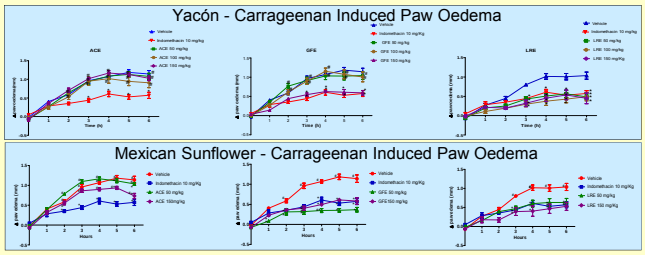
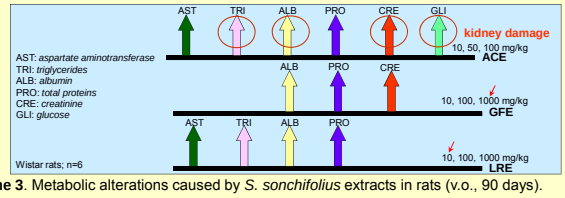


Figure 3. Paw oedema assay in BALC/c mice (n=6). *P<0.05 *vs.* vehicle. #P<0.05 *vs.* indomethacin.



Scheme 3. Metabolic alterations caused by *S. sonchifolius* extracts in rats (v.o., 90 days).

Conclusions: Our results strongly suggest that not only STLs are involved in the anti-inflammatory activity and that their occurrence in these medicinal plants cause toxicity. Using the metabolite profiling approach it was possible to find out which classes of compounds are related to a certain biological property. These findings are very important due to the medicinal and/or toxic properties of these species and their leaf infusion used in folk medicine.

Acknowledgements

USP Universidade de São Paulo · CNPq · FAPESP · CAPES