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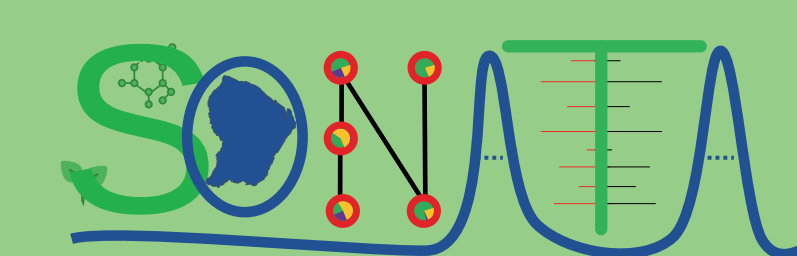
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Exploring the anti-mycobacterial potential of French Guiana's flora through a metabolomic study

Célia BREAUD^{1*}, Clémentine SAUNIER², Stéphane CANAAN², Béatrice BAGHDIKIAN¹, Sok-Siya BUN-LLOPET¹ and Elnur GARAYEV¹

Aix Marseille Univ, CNRS 7263, IRD 237, Avignon Université, IMBE, 27 blvd Jean Moulin, Service of Pharmacognosy and Ethnopharmacology, Faculty of Pharmacy, 13385 Marseille, France
Aix Marseille Univ, CNRS, LISM UMR 7255, IMM FR3479, 13402 Marseille, France
*email: celia.breaud@imbe.fr



Context

Within the plant diversity of French Guiana's, many species are used by local populations for medicinal purposes. These plants, and their associated traditional uses, have been the subject of numerous census studies, and have attracted the attention of scientists for their therapeutic potential, particularly in the treatment of infectious diseases.

Bacterial infections such as tuberculosis (TB), caused by *Mycobacterium tuberculosis*, are a major public health problem in French Guiana. With a high incidence rate and the emergence of drug-resistant strains, there is an urgent need to explore therapeutic alternatives [1-2]. Local traditional knowledge could be a source of discovery for new anti-TB agents.

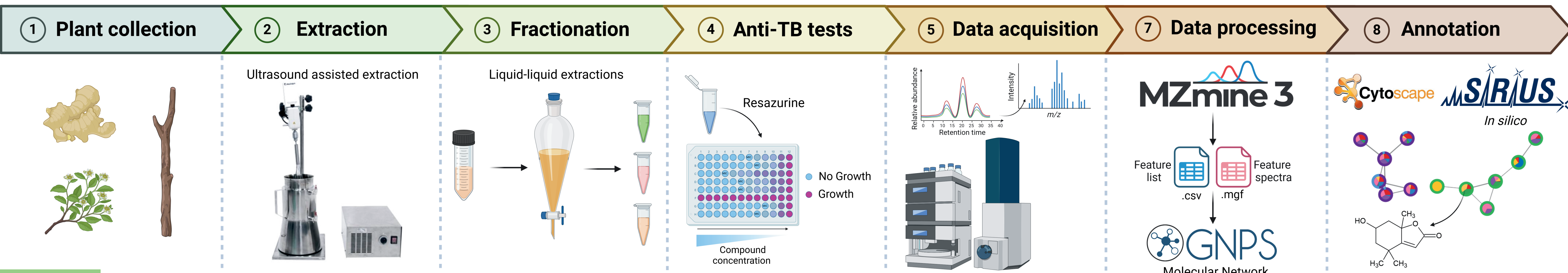


Objectives

In drug discovery from natural products, it can be challenging to describe the metabolites responsible for the biological activity. The use of the **Mass Spectrometry based Molecular Network** approach can facilitate structural dereplication and accelerate the annotation of structural entities in complex samples.

This study aims to facilitate the characterization of bioactive metabolites responsible for the anti-TB activity present in **9 plant species** from French Guiana.

Based on the literature, preliminary results indicate interesting activities for the plant species selected [3]. Some are also used in traditional medicine to treat tuberculosis symptoms (fever, cough, asthenia).



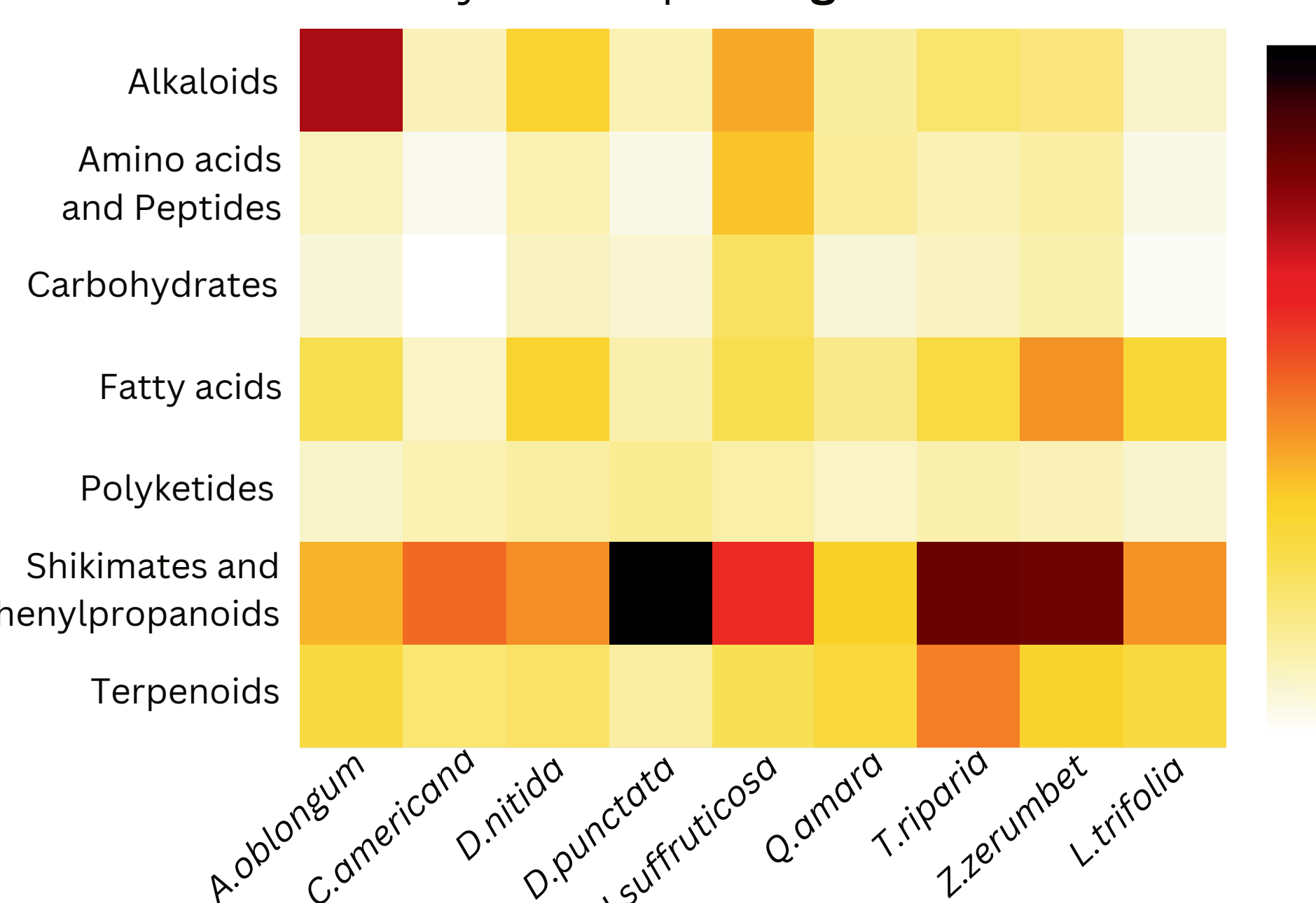
Results

1 Chemodiversity

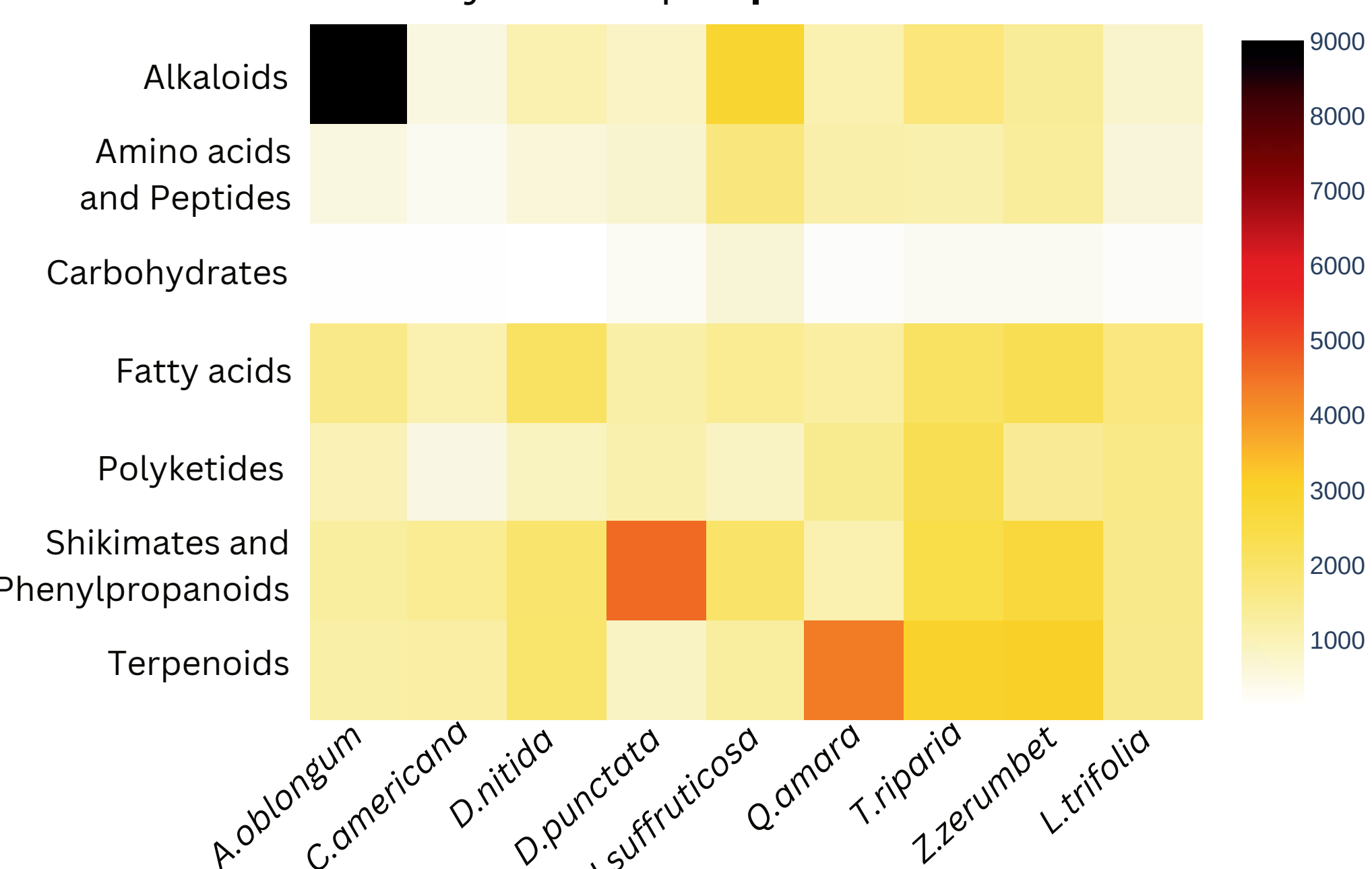


- Heatmaps were constructed based on the *in silico* prediction by CANOPUS module of the SIRIUS 5 software, and according to the **chemical pathways** from NPClassifier.
- The studied species contain mainly metabolites of the **shikimates and phenylpropanoids pathway**: a large number of flavonoids and isoflavonoids were annotated.
- T. riparia* and *Q. amara* are rich in **terpenoids**
- A. oblongum* contains mainly **alkaloids**, specially of the **tryptophan type**.

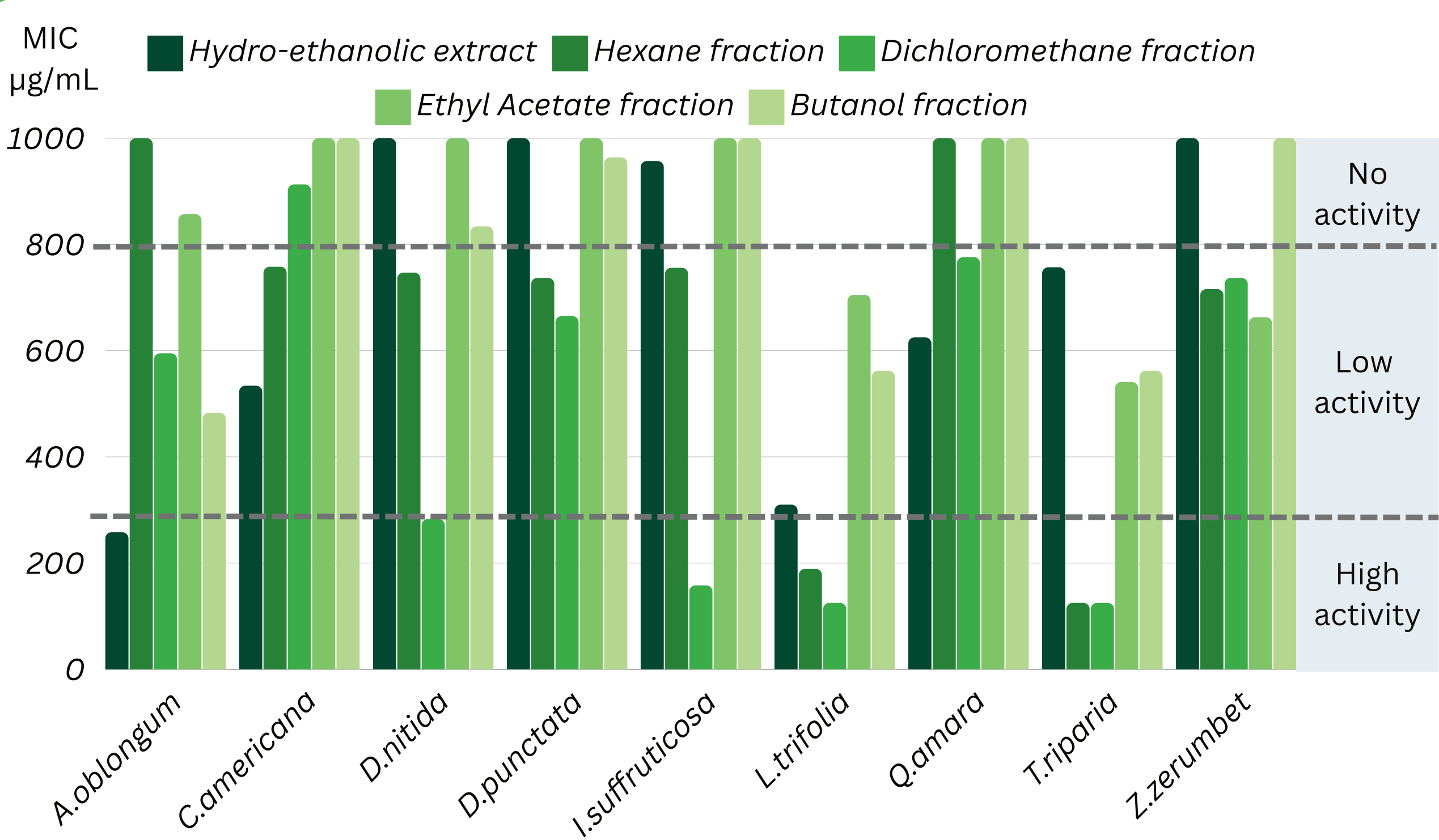
Pathway heatmap in **negative** ionisation mode



Pathway heatmap in **positive** ionisation mode

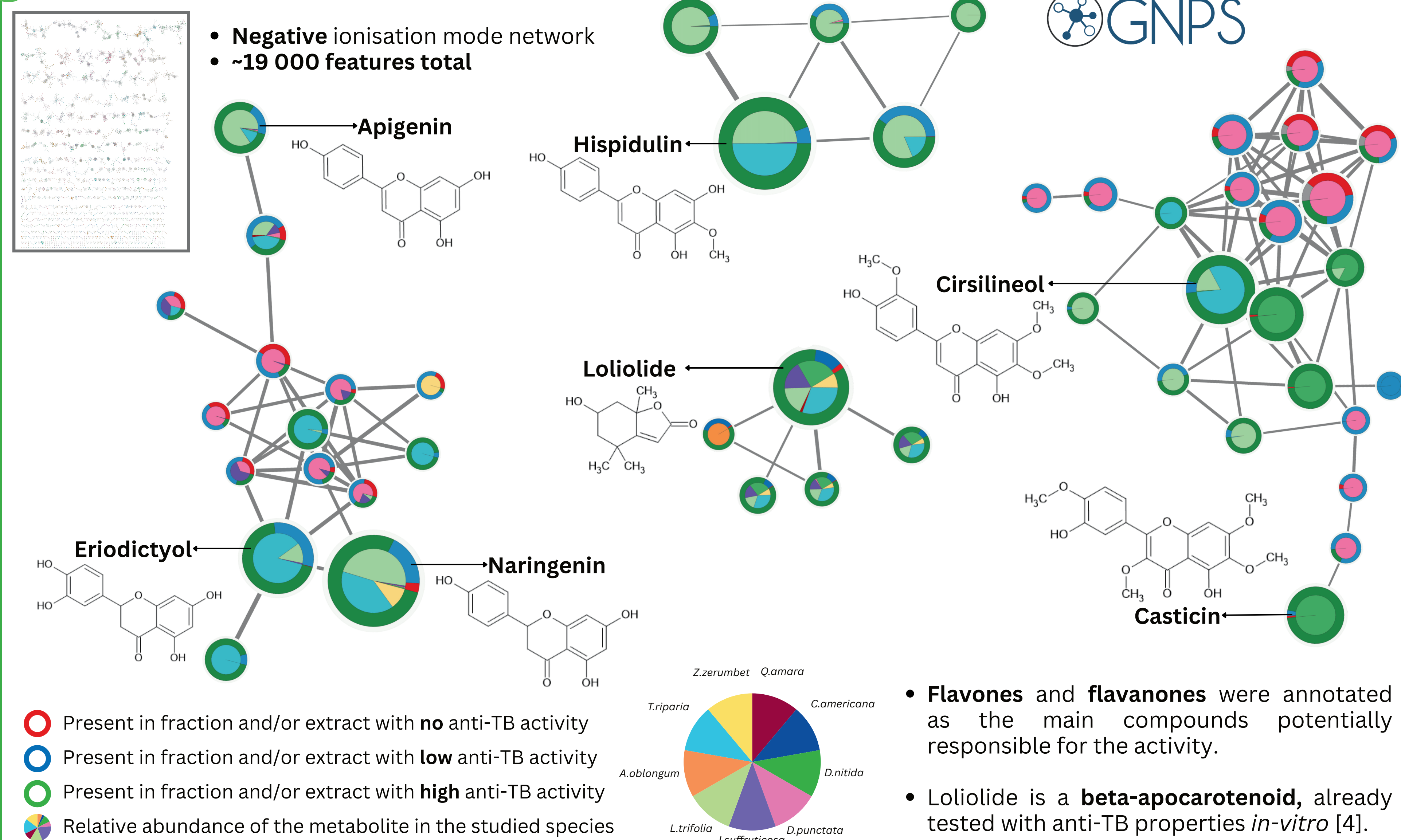


2 Biological assays



- Anti-tuberculosis activities of crude extracts and fractions were evaluated *in vitro*. MIC₅₀ were determined using **resazurin microtiter assay** (classic REMA), a colorimetric liquid culture-based drug susceptibility assay for *Mycobacterium tuberculosis* (MTB).
- Threshold for high activity: **MIC₅₀ < 250 µg/mL**.
- Fractionation allowed to detect activities that were not detected in crude extracts. The apolar fractions (hexane and dichloromethane) of *I. suffruticosa*, *L. trifolia* and *T. riparia* were tested with strong activities against MTB.

3 Molecular Network



- Negative ionisation mode network**
- ~19 000 features total**
- Present in fraction and/or extract with **no** anti-TB activity
- Present in fraction and/or extract with **low** anti-TB activity
- Present in fraction and/or extract with **high** anti-TB activity
- Relative abundance of the metabolite in the studied species

- Flavones and flavanones** were annotated as the main compounds potentially responsible for the activity.
- Loliolide is a **beta-apocarotenoid**, already tested with anti-TB properties *in-vitro* [4].

Conclusion

The present experimental and analytical workflow allow us to prioritise data of biological interest, and annotate metabolites potentially responsible for the anti-TB properties in complex samples.

- Multiple flavonoids, of the **flavone** class, were annotated as potential new antitubercular compounds.
- Targeted purification of the proposed metabolites, coupled with NMR analysis will allow to confirm the proposed structures.
- Anti-TB assays will also be performed on isolated compounds to evaluate their activity.

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