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New strategy in the discovery of natural antituberculosis agents from French Guiana flora

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Plants have been used for centuries in traditional medicine, and are widely studied by chemists for their molecular diversity. Ethnopharmacology aims to valorize traditional knowledge on plants, as they represent an important source of new compounds of therapeutic interest.

Context

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, poses a major threat to public health, especially in middle and low-income countries. There are a limited number of medications available to treat tuberculosis; additionally, multi-drug resistant and extensively-drug resistant TB strains are becoming more prevalent [1]. In France, French Guiana is the region with the highest reporting rate of tuberculosis disease cases [2].

Among traditional uses in French Guiana, various plant species are used to treat tuberculosis symptoms. Previous research have confirmed the anti-TB activity of a number of species, but very few led to the identification of metabolites responsible for this activity [3,4].



Objectives

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

This workflow aims to facilitate the characterization of bioactive metabolites responsible for the anti-TB activity present in 12 plant species from French Guiana.

TB incidence in 2021 : **25.5 cases/100 000 habitants** [2]



Main steps

1) Sample preparation

Two types of extracts : Ultrasound assisted extraction in a hydro-ethanolic solvent mixture (70/30 v/v) and aqueous decoction, which is the traditional method of preparation. Further fractionation of both extracts using liquid-liquid extraction, with 4 solvents of increasing polarities, to concentrate potential bioactive metabolites.

2) Sample library building

Sampling in 96 deepwell inserts plates at a precise concentration, for rapid and easy access of the samples. Drying under nitrogen gas and storage at -20°C.

3) Metabolomics

Data acquisition using UHPLC-HRMS/MS, and Molecular network building. GC-MS and NMR data allow further annotation of the fractions.

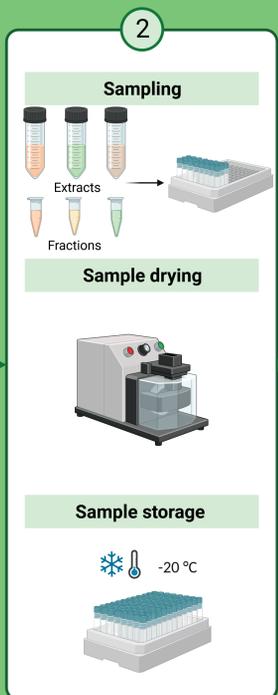
4) Activity and Purification

Fragment-based selection of active features using a pharmacophoric model built on available treatment against TB. Testing of extracts and fractions against TB with determination of minimum inhibitory concentration. Purification of potential bioactive metabolites.

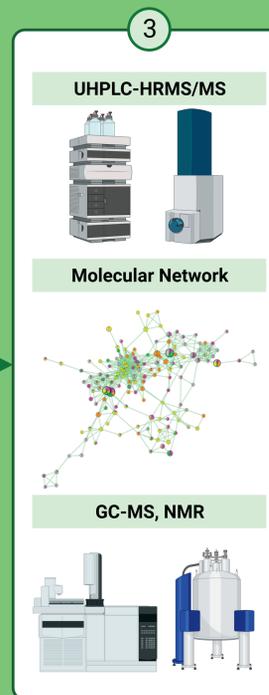
Sample preparation



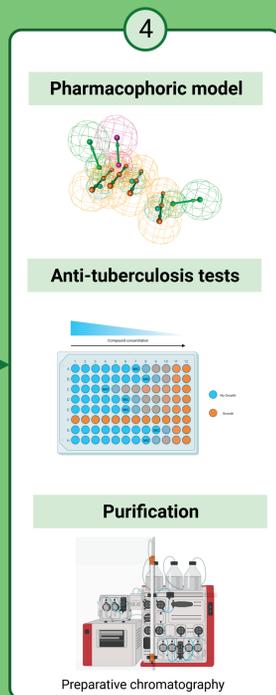
Sample library building



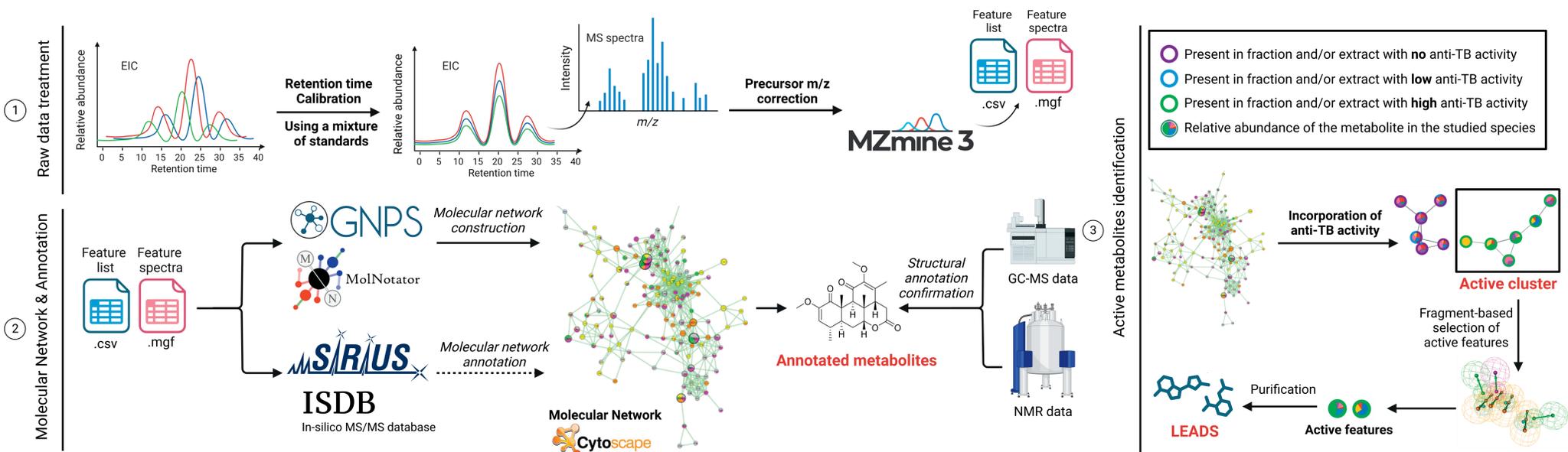
Metabolomics



Activity & Purification



Metabolomics workflow



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