
Targeting antimicrobial compounds in boswellia resin described in a tuberculosis remedy from arab medieval pharmacopeia

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Résumé

Antimicrobial resistance (AMR) has emerged as a major public health threat in the 21st century, being associated with an estimated 4.95 million deaths in 2019. To address AMR, the World Health Organization has published a bacterial priority pathogens list, in which rifampicin resistant *Mycobacterium tuberculosis* is classified as 'critical' - the highest priority - due to the lack of effective treatments and the increasing emergence of resistance to existing antibiotics (1). In response to this growing threat, the discovery of new antimycobacterial drugs has become crucial.

Ethnopharmacognosy focuses on traditional medicines to identify bioactive molecules that have not yet been described. This traditional knowledge can provide valuable resources for current research (2). A consortium of scientists, including historians, microbiologists, chemists, and bioinformaticians, has developed a database from Arab Medieval Pharmacopoeia to search for potential active ingredients (3). This work led to the identification of a remedy used in the 9th Century to treat scrofula, a skin and mucous membrane infections caused by *M. tuberculosis.* The remedy consists of 8 plants and 2 metals, including resins of *Boswellia* genus, also called frankincense. Frankincense, which are rich in terpenoids compounds and known for its anti-inflammatory properties, has been described in Ibn Sina's Canon of Medicine to treat tuberculosis (4).

In this research, we studied *Boswellia* resins antibacterial activity and targeted potentially active molecules by bio-guided fractionation and Features Based-Molecular Networking. After fractionation of the frankincense ethyl acetate extract, two fractions showed antibacterial activity against *M. tuberculosis* H37Rv (MIC value < 200 μg/mL) while three showed antibacterial activity against Gram positive *Staphylococcus aureus* HG001 (MIC value < 100

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*Intervenant

μg/mL), *Staphylococcus epidermis* ATCC14990 (MIC value $<$ 50 μg/mL) and *Bacillus subtilis* ATCC23857 (MIC value $<$ 20 μg/mL). To determine which molecular families are present in these fractions, a dereplicative approach based on HPLC-HRMS/MS data was performed, confirming the presence of sesqui and diterpenes. In addition, pharmacophoric deconvolution - an innovative differential analysis of 2D NMR spectra correlated with antibacterial activity - is currently underway to specifically identify the pharmacophores from these fractions and accelerate their isolation and their structure identification.

Mots-Clés: Boswellia, Antibacterial, Tuberculosis, Molecular Networking