In silico comparison of antimycobacterial natural products with known antituberculosis drugs

Marlene Espinoza-Moraga, Nicholas M Njuguna, Grace Mugumbate, Julio Caballero, Kelly Chibale

Abstract

The chemical space based on physicochemical properties and structural features of a diverse group of natural products with reported in vitro activity against different Mycobacterium tuberculosis strains is investigated using in silico tools. This is compared to the chemical space occupied by drugs currently recommended for the treatment of various forms of tuberculosis as well as compounds in preclinical and clinical development. Docking studies exploring possible binding affinities and modes of two main clusters of natural products on two different mycobacterial targets are also reported. Our docking results suggest that scytoscalarol, an antibacterial and antifungal guanidine-bearing sesterterpene, can inhibit arabinosyltransferase Mtb EmbC, and the β-carboline alkaloids 8-hydroxymanzamine A and manzamine A can bind to the oxidoreductase of Mtb INHA. On this basis, these products showing high binding affinities to the two targets in silico could be rationally selected for in vitro testing against these targets and/or semisynthetic modification.