Evaluation of the antitubercular potential of sesquiterpene lactones against *Micobacterium tuberculosis*

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Introduction

Natural products (NP) are a large group of substances, commonly found in animals, plants and microorganisms, and usually displaying interesting biological activity. The sesquiterpene lactones (SLs) may be mentioned as examples of active compounds. This is a class of NP with high structural variability and with activities such as antibacterial, antifungal, antitumor, among others. Some SL are Lychnofolide (**1**), Goyazensolide (**2**) and Goyazesolide acetate (**3**).

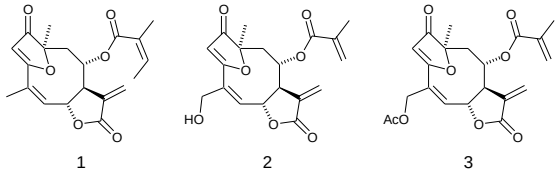

Figure 1: Structures of the sesquiterpene lactones.

Tuberculosis (TB) is an airborne contagious disease caused by *Mycobacterium tuberculosis*. This disease affects mainly lungs and killed 1.5 million people in 2013.[1,2] In the same year, 9 million people fell ill with TB, which is one of the top killers of women in reproductive age.[1] Due to our research interests in SL and biological activities, we decided to test some natural and modified SL against *M. tuberculosis*.

Results and Discussion

The SL, **1**, was isolated from the dichloromethane (DCM) rinse extract prepared from *Eremanthus matogrossensis*. An amount of 500 g of dried leaves was washed with DCM and the solvent was evaporated to give the extract. Column chromatography was used to purify the Lychnofolide (**1**), which was identified by ^{1}H and ^{13}C NMR. Goyazensolide (**2**) was previously isolated in our research group. This SL was submitted to a chemical transformation to give its acetate (**3**).[3,4] Again, chromatography and NMR were resources to purify and characterize, respectively, the product. The three SL were assayed against *M. tuberculosis* in the Microbiology Laboratory in our University. The activity was determined by the minimum inhibitory concentration (MIC). The procedure for MIC determination used is recommended by the Clinical and Laboratory Standards Institute (CLSI). Dimethyl-sulfoxide (DMSO) was used to dissolve the substances before addition of Mueller Hinton broth. DMSO was also used as negative control. The bacterial growth was verified by the use of resazurin: the blue coloration indicating lack of bacterial growth. The results obtained for the three SLs are shown on Table 1.

Table 1: SLs results against *M. tuberculosis*.

Compounds assayed:	**1**	**2**	**3**
MIC (μg.mL^{-1})	7,8	62,5	6,25

According to Cantrell and his coworkers,[5] a substance with MIC of 64 μg.mL^{-1} against mycobacteria is considered to have moderate activity. This is the case of the natural SL **2.** The natural SL **1** has a much better MIC value against *M. tuberculosis*. Finally, the transformation of SL **2** in compound **3** led to an activity much better than the displayed by the natural lactone.

Conclusion

One can conclude that these SLs are active against *M. tuberculosis*. Nevertheless, some differences in structure can provide activities in different magnitude. The importance of structural modification in the search for more active compounds is very clear in this work.

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