Background

The need to overcome the emergence of multidrug- and extensively-drug-resistant strains of Mycobacterium tuberculosis has triggered the exploration of novel and unconventional approaches to control microbial infections. One major component of resistance to many classes of antimicrobials is multidrug efflux, and efflux mechanisms significantly contribute to antibiotic resistance in mycobacteria. The activation of multidrug efflux pumps also plays a role in biofilm formation and it is suggested to be responsible for the enhanced antibiotic resistance of biofilms. The identification of efflux pump inhibitors is therefore an attractive lead in designing new anti-tubercular therapy as well as reversing the resistance. Plants play a major role in drug discovery by providing bioactive scaffolds against a variety of targets. The genus Allium are well-known worldwide as spices, ornamental plants, but most importantly for their medicinal properties. Synthetic analogues based on the structure of bioactive natural products Allium stipitatum were produced to develop an antibacterial activity.

Objectives

The objective of this research was to synthesize analogues of natural product disulphides isolated and characterized from Allium stipitatum Regel and evaluate their possible efflux pump inhibition and biofilm inhibition in mycobacteria, fungi and other Gram positive and negative microorganisms.

Materials and Methods

The synthetic analogues inhibited the growth of different Mycobacterium species more than Gram-negative, Gram-positive and fungal species and showed inhibitory effect in the EPI assay and also dose dependent inhibited biofilm formation, revealing their possible endogenous mechanisms of action although further studies is required. They also did not significantly affect the viability of the murine macrophage cells. These findings indicate that compounds structurally related to naturally-occurring disulphides can serve as leads for the identification of novel scaffolds for the development of effective new antymycobacterials.

Conclusions

References