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2-AMINO ALKANOLS AND ALKYL-1,2-DIAMINES AS POTENTIAL ANTIMYCOBACTERIAL AGENTS

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INTRODUCTION

Tuberculosis (TB) is an infectious disease caused mainly by *Mycobacterium tuberculosis* (MTB). TB is a major public health problem worldwide and for the past 5 years it has led as one of the top 10 causes of death caused by a single infectious agent and the ninth leading cause of death worldwide (Global tuberculosis report. 2021). Furthermore, the lack of new drugs and the occurrence of multidrug-resistant strains (MDR) require the development of new drugs and treatment strategies (Conradie et al. 2020, N. Engl. J. Med). The aim of the present study was to design and synthesize new derivatives related to dihydrosphingosine and ethambutol and to evaluate their *in vitro* TB activity against susceptible and multiresistant MTB strains.

MATERIAL AND METHODS

Two families of compounds were obtained: 2-amino alkanol (**type I**) and alkyl-1,2-diamine (**type II**). The synthesis began with the obtaining of alkyl α-amino acids, the amino group was protected as a carbamate (Boc) and the acid group was reduced to alcohol to obtain the Boc-amino alkanols. Then, the alcohol group was protected as a benzyl (Bn) and the Boc-carbamate was removed. The free amine was then alkylated with different aliphatic fragments, and finally the Bn was removed to give compounds type I. On the other hand, the Boc-amino alkanol was converted to an amine in a three-step procedure. The primary amine obtained was alkylated and the Boc removed to give compounds type II (Olmo et al. 2016, Arch. Med Res).
Compounds type I and II were evaluated *in vitro* against MTB strains, H37Rv (sensitive) and 1576 (multiresistant), using ethambutol as the reference drug.

RESULTS

Twenty-five type I compounds and sixteen of type II were synthesized, purified and characterized. Its antimycobacterial activity as well as the cytotoxicity in three mammalian cell lines were determined, in order to achieve the selectivity index (SI). The most potent compounds showed 2- to 14-fold potency over ethambutol in the MDR strain, and the SI ranged from 2.2 to 82.2.

CONCLUSIONS

More than 10 derivatives were more potent than ethambutol *in vitro*. Perhaps, they can be considered as new drug candidates.

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