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Synthesis of new fatty acid amides derivates of castor oil with antituberculosis activity

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Introduction: Tuberculosis (TB) is a contagious disease caused by *Mycobacterium tuberculosis*. According to reports of the World Health Organization (WHO) 30% of the world's population is infected, although only 10% display symptoms. In Mexico, each year 18 000 new cases and more than 2000 deaths from TB are recorded. In order to surpass this disease, WHO's program "The global plan to stop TB 2011-2015", defines several strategies to eradicate TB worldwide, including the development of new drugs with fewer side effects and increased activity on drug resistant strains. Our research group decided to carry out the synthesis and bactericidal evaluation on strains of M. tuberculosis, of several new cyclic amides analogous to pyrrolidin ricinoleilamide, a compound which was recently described as a micobactericidal agent.

Methodology: The synthesis of target amides was performed by MeOH-KOHtrans-esterification of castor oil to methyl ricinoleate, which, after DHP protection and enzymatic hydrolysis generated 12-THP-ricinoleicacid. The desired new amides were obtained by coupling of 12-THP-ricinoleic acid with different amines via the mixed anhydride method, and hydrolysis of the protecting group (scheme 1). The bactericidal effect of the new amides was evaluated on the strain of M. tuberculosis H37 Ra (non-virulent), obtained from the American collection (ATCC). Bacterial growth was monitored by the resazurin method, which is based on the metabolic activity. Bactericidal effect of new compounds was compared with isoniazid and rifampicin, antibiotics used to treat TB. From the results, the minimum inhibitory concentration (MIC) was determined.

Results and discussion: The synthesis of the amides was obtained with an overall yield of 55-60% based on castor oil. The tested compounds showed activity against the strain of Mycobacterium tuberculosis H37Ra. Comparing the values obtained for protected amides with the tetrahydropyranyl group and do not exhibit a significant difference is observed in the bactericidal activity

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