STUDY OF STRUCTURE-ACTIVITY RELATIONSHIP OF A SERIE OF MOLECULES PRESENT IN ESSENTIAL OILS WITH ANTIMYCOBACTERIAL ACTIVITY AGAINST STRAIN OF *Mycobacterium bovis* AN-5.

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Introduction. Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (Mtb). The World Health Organization has stated that one third of the world population is infected with this organism and is responsible for the deaths of just over one million people (1). Because of this, there is now an interest in finding natural products as antimicrobial agents. Essential oils (EOs) are water insoluble chemicals and with a variety of compounds mainly terpenes (2). Interest in the use of EOs is due to its broad-spectrum antimicrobial agents (3). This has motivated the search for approaches that minimize the efforts of synthetic and biological assessment for the discovery and development of new compounds with pharmacological potential. QSAR studies assume that there is a relationship between biological activity of a molecule and its structure, trying to establish a simple mathematical relationship to reproduce (and subsequently predict) an activity for a set of composite. The objective of this study is to generate a mathematical equation to describe and predict subsequent antimycobacterial activity of the search for new molecules and the design of new antimycobacterial agents.

Methods. The Minimum Inhibitory Concentration (MIC) was tested on twenty terpenoids in the strain of *Mycobacterium bovis* AN-5 by the Alamar Blue technique, detection technique based on colorimetric change caused by cell growth. The compounds to be evaluated were purchased through Sigma-Aldrich distributor. Molecular systems were built and optimized to a level DFT using B3LYP functional and a base assembly 6-31G. Once optimized systems proceed to calculate molecular descriptors, topological, structural and quantum. With the set of descriptors was performed numerous linear multiple regressions, using statistically satisfactory model based on the regression coefficient (r^2), standard deviation (s) and the statistic F. Once selected the four descriptors that had the highest predictive power was built prediction model (Equation 1).

Results. The MIC of the compounds was tested in triplicate demonstrating the high efficiency of terpenoids as antituberculosis agents, obtaining results as thymol has a MIC of 1.52 ug/ml or 6.25 carvacrol ug/ml. The minimum inhibitory concentration (MIC) of the 20 terpenes are given in Table 1.

Table. 1. Minimum Inhibitory Concentration of the compounds tested against Mycobacterium bovis strain AN-5.

No.	Compounds	MIC	No.	Compounds	MIC
1	Anisaldehyde	6.25	11	Limonene	50
2	β pinene	50	12	Linalol	25
3	Carvacrol	6.25	13	Mentol	75
4	Carvone	50	14	Mircene	25
5	Cinnamaldehyde	12.5	15	Terpinolene	25
6	Cuminaldehyde	25	16	Thymol	1.52
7	Estragol	25	17	Vainillina	6.25
8	Eucalyptol	50	18	Vainillona	- -
9	Eugenol	25	19	Cinamic Acid	25
10	Geraniol	12.5	20	Citronelol	12.5

The MIC are expressed in ug/ml. Analysis was performed in triplicate for MIC determination.

Among the descriptors selected by the multiple linear regression model to predict the antimycobacterial activity are water partition coefficient/octanol (LogP), water solvation energy (ΔG_{solv}), molar refractivity (MR) and the unsaturation (Ui). The calculation of the mathematical model is expressed in Equation 1.

$$\text{LogMIC} = 0.0837(\text{AlogP}) + 0.0646(\Delta G_{solv}) - 0.0637(\text{RM}) - 0.1499(\text{Ui}) - 5.1882$$

$n = 19$ $r^2 = 77.07$ $Q^2 = 52.09$ $s = 0.212$ $F = 9.2$

Conclusions. The properties of importance in the present study appear to be linked to the degree of solubility of the terpenoids in the lipid layer of the cell wall. It is noteworthy that the cell wall of mycobacteria are highly lipophilic, they contain a high concentration of mycolic acids in it. Therefore exposed conceptualize the model presented shows that statistically significant, and therefore, has an ability to predict new antituberculosis activity of chemical structures.

References.

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