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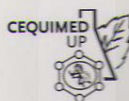
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**TUBERCULOSTATIC ACTIVITY OF MARINE SESQUITERPENE
(S)-(+)-CURCUPHENOL AND SEMISYNTHETIC DERIVATIVES**

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Abstract

The human disease tuberculosis (TB) still remains a leading cause of death in the world. This is due partly to its synergy with HIV and to the emergence of multidrug and extensive drugresistance (MDR and XDR) strains of *Mycobacterium tuberculosis* [1].

Natural products continue to play a dominant role in the drug discovery for the treatment of human diseases [2]. Marine sponges are a valuable source for the search of new anti-tuberculosis agents since several sponge metabolites have been reported as tuberculostatic [3].

(S)-(+)-Curcuphenol and (S)-(+)-curcudiol are biologically active bisabolene sesquiterpenoids that have been isolated from the marine sponge *Didiscus oxeata* [4]. (S)-(+)-Curcuphenol exhibits a wide spectrum of activities and a recent study by Hamann *et al.* referred that phenol substituted analogs of (S)-(+)-curcuphenol exhibited moderated *M. tuberculosis* (H37Rv) activity [5].

As part of an ongoing effort to discover new anti-tubercular agents from marine sponges, we report here the biological evaluation of the natural sponge sesquiterpenes (S)-(+)-curcudiol and (S)-(+)-curcuphenol, together with some curcuphenol semisynthetic derivatives [4], against the susceptible and resistant *M. tuberculosis* strains. Six out of eight sesquiterpenes tested show moderate activity (MIC 12.5-100.0 µg/mL). Our results suggested that the introduction of an oxygenated function such as epoxide or one or two hydroxyl groups in the double bound of the side chain of (S)-(+)-curcuphenol, decrease the antimycobacterial activity. Inversely there is an increase of *M. tuberculosis* inhibition, if the substituent is an alkoxy group. The presence of a chlorine atom at aromatic ring of (S)-(+)-curcuphenol does not appear to influence the growth of the *M. tuberculosis* (H37Rv).

References

- [1] B.R., Copp, A.N., Pearce, *Nat. Prod. Rep.*, 2007, 24, 278-297.
- [2] D. J. Newman, G. M. Cragg, *J. Nat. Prod.* 2007, 70, 461-477.
- [3] A. M. S. Mayer, A. D. Rodriguez, R. G. S. Berlinck, M. T. Hamann, *Comp. Biochem. Physiol. Part C Pharmacol. Toxicol.* 2007, 145, 553-581.
- [4] H. Gaspar, C. Moiteiro, J. Sardinha, A. González-Coloma, *Nat. Prod. Comm.* 2008, 3(9), 1457-1464.
- [5] W. Gul, N.L. Hammond, M. Yousaf, J. Peng, A. Holley, M. T. Hamann, *Biochimica Biophysica Acta* 2007, 1770, 1513-1519.

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