

Accepted Manuscript

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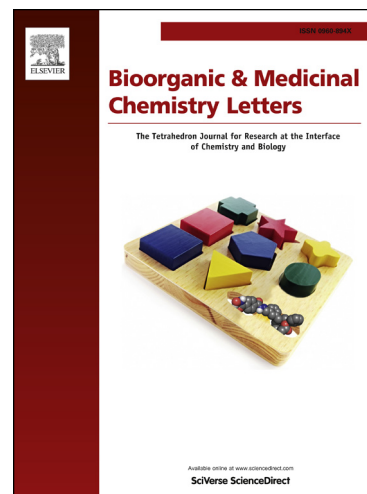
PII: S0960-894X(13)01136-0
DOI: <http://dx.doi.org/10.1016/j.bmcl.2013.09.062>
Reference: BMCL 20914

To appear in: *Bioorganic & Medicinal Chemistry Letters*

Received Date: 23 August 2013
Revised Date: 20 September 2013
Accepted Date: 23 September 2013

Please cite this article as: Faria, J.V., dos Santos, M.S., Bernardino, A.M.R., Becker, K.M., Machado, G.M.C., Rodrigues, R.F., Canto-Cavalheiro, M.M., Leon, L.L., Synthesis and activity of novel tetrazole compounds and their pyrazole-4-carbonitrile precursors against *Leishmania* spp, *Bioorganic & Medicinal Chemistry Letters* (2013), doi: <http://dx.doi.org/10.1016/j.bmcl.2013.09.062>

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Synthesis and activity of novel tetrazole compounds and their pyrazole-4-carbonitrile precursors against *Leishmania spp.*

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ABSTRACT

A new series of 5-(1-aryl-3-methyl-1H-pyrazol-4-yl)-1H-tetrazole derivatives (**4a-m**) and their precursor 1-aryl-3-methyl-1H-pyrazole-4-carbonitriles (**3a-m**) were synthesized and evaluated as antileishmanials against *Leishmania braziliensis* and *Leishmania amazonensis* promastigotes *in vitro*. In parallel, the cytotoxicity of these compounds was evaluated on the RAW 264.7 cell line. The results showed that among the assayed compounds the substituted 3-chlorophenyl (**4a**) ($IC_{50}/24h = 15 \pm 0.14 \mu M$) and 3,4-dichlorophenyl tetrazoles (**4d**) ($IC_{50}/24h = 26 \pm 0.09 \mu M$) were the most potent against *L. braziliensis* promastigotes, as compared the reference drug pentamidine, which presented $IC_{50} = 13 \pm 0.04 \mu M$. In addition, **4a** and **4d** derivatives were less cytotoxic than pentamidine. However, these tetrazole derivatives (**4**) and pyrazole-4-carbonitriles precursors (**3**) differ against each of the tested species and were more effective against *L. braziliensis* than on *L. amazonensis*.

Keywords: Antileishmanial activity, *Leishmania braziliensis*, *Leishmania amazonensis*, Tetrazole

The parasitic protozoans of the genus *Leishmania* are the causative agents of several forms of cutaneous, mucocutaneous, and visceral leishmaniasis. It is transmitted to human beings and other mammals by the bite of an infected female Phlebotomine sandfly.¹ *Leishmania* has two evolutive forms: an extracellular flagellated promastigotes within the Phlebotomine vector and the intracellular amastigotes within mononuclear phagocytes in mammalian host. According to WHO estimations, leishmaniasis affect almost 12 million people in 88 countries on five continents (Africa, Asia, Europe, North and South America), representing

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