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Abstract

In Vitro Primary Screening of a Synthetic Series of Chromenoazoldiones against *Trypanosoma cruzi* †

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Similarities between parasites and cancer have prompted parasitologists to take advantage of several approaches enabled by cancer research to identify antiparasitic agents [1]. Quinones generate reactive oxygen species (ROS), which not only results in their antitumor properties, but also in a mechanism for designing antichagasic drugs. Here, a synthetic series of seven chromenoazoldiones previously defined as potential antitumorals [2,3], has been assayed in vitro against *Trypanosoma cruzi* (CL-B5 *lacZ* strain) in a primary screening that evaluates activity over epimastigotes and toxicity on L929 cells [4,5]. Compounds PM199, PM203 and PM401 achieved higher IC_{50} values than that of the reference drug benznidazole (BZ): IC_{50} = 14.45 ± 1.90, 14.84 ± 4.49, 16.01 ± 9.06 and 36.47 ± 4.43 μM (PM199, PM203, PM401 and BZ, respectively). However, their higher cytotoxicity led to a lower selectivity (SI) on epimastigotes: SI_{PM199} = 5.83, SI_{PM203} = 7.03, SI_{PM401} = 5.27 and SI_{BZ} > 7.02. Only two compounds showed no cytotoxicity (LC_{50} > 256 μM) and thus, no derivative was further assayed against intracellular amastigotes. These chromenoazoldiones did not show relevant activity on *T. cruzi*. Their cytotoxicity, probably connected to ROS production in mammalian cells, encourages further optimization to apply them as trypanocidal templates.

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References

1. Oliveira, G. Cancer and parasitic infections: Similarities and opportunities for the development of new control tools. *Rev. Soc. Bras. Med. Trop.* **2015**, *47*, 1–2.
2. Morales, P.; Vara, D.; Gómez-Cañas, M.; Zúñiga, M.C.; Olea-Azar, C.; Goya, P.; Fernández-Ruiz, J.; Díaz-Laviada, I.; Jagerovic, N. Synthetic cannabinoid quinones: preparation, *in vitro* antiproliferative effects and *in vivo* prostate antitumor activity. *Eur. J. Med. Chem.* **2013**, *70*, 111–119.
3. Morales, P.; Blasco-Benito, S.; Andradas, C.; Gómez-Cañas, M.; Flores, J.M.; Goya, P.; Fernández-Ruiz, J.; Sánchez, C.; Jagerovic, N. Selective, nontoxic CB2 cannabinoid o-quinone with *in vivo* activity against triple-negative breast cancer. *J. Med. Chem.* **2015**, *58*, 2256–2264.

4. Fonseca-Berzal, C.; Merchán Arenas, D.R.; Romero Bohórquez, A.R.; Escario, J.A.; Kouznetsov, V.V.; Gómez-Barrio, A. Selective activity of 2,4-diaryl-1,2,3,4 tetrahydroquinolines on *Trypanosoma cruzi* epimastigotes and amastigotes expressing β-galactosidase. *Bioorg. Med. Chem. Lett.* **2013,** *23,* 4851–4856.
5. Fonseca-Berzal, C.; Ibáñez-Escribano, A.; Reviriego, F.; Cumella, J.; Morales, P.; Jagerovic, N.; Nogal-Ruiz, J.J.; Escario, J.A.; da Silva, P.B.; Soeiro, M.N.C.; Gómez-Barrio, A.; Arán, V.J. Antichagasic and trichomonacidal activity of 1-substituted 2-benzyl-5-nitroindazolin-3-ones and 3-alkoxy-2-benzyl-5-nitro-2*H*-indazoles. *Eur. J. Med. Chem*. **2016**, *115,* 295–310.