SEPTEMBER 23-27 2024
19BMOS
BRAZILIAN MEETING ON ORGANIC SYNTHESIS
BENTO GONÇALVES, RS - BRAZIL

Synthesis of new marinoquinoline derivatives with potential antimalarial activity

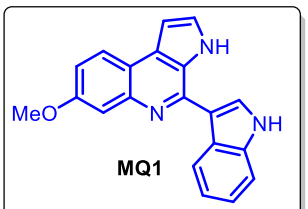
Wellington da Silva[1*], Guilherme Eduardo de Souza[2], Rafael Victorio Carvalho Guido[2], Matthew Houghton Todd[3] and Carlos Roque Duarte Correia[1]

1) Institute of Chemistry, State University of Campinas, UNICAMP, Campinas, Brazil
2) Institute of Physics of São Carlos, University of São Paulo, USP, São Carlos, Brazil
3) School of Pharmacy, University College London, UCL, London, England, United Kingdom
****e-mail: wellingtondasilva1804@gmail.com***

Keywords: *Malaria, Synthesis, Marinoquinolines.*

ABSTRACT

Malaria is a disease caused by species of the parasite *Plasmodium* spp,[1] which only in 2022 caused the deaths of 608,000 people. Currently, there are drugs available for the treatment of malaria, however, the parasites are gaining resistance to them, thus making the treatment ineffective.[2] Therefore, the development of new drugs capable of combating this disease is urgent. In this context of new drug discovery, a class of compounds called marinoquinolines (MQs) has been gaining prominence due to their inhibitory activities against *Plasmodium*.[3] Based on the structure of MQ1, previously synthesized by Professor Correia's group, it was decided to make new modifications to the indole portion of this substance, aiming to obtain more potent substances. Until now, 32 marinoquinolines have been synthesized from a synthetic route of 7 to 10 steps, of which 82% were active against *P. falciparum* 3D7, with IC_{50} values ranging from 320 nM to 5.9 µM.



MQ1

IC_{50} (*P. falciparum* 3D7) = 2.09 ± 0.09 µM

ACKNOWLEDGEMENTS

We acknowledge the São Paulo State Research Support Foundation (FAPESP, grants 2014/25770-6; 2013/07600-3, and 2023/00383-9), the Brazilian National Research Council (CNPq, grant 306773/2018-0),) for the fellowship to Wellington da Silva (grants 2022/03731-5, and 2023/03295-3) and Medicines for Malaria Venture.

REFERENCES

(1) Kumar, S.; Bhardwaj, T. R.; Prasad, D. N.; Singh, R. K. Drug Targets for Resistant Malaria: Historic to Future Perspectives. *Biomed. Pharmacother.* **2018**, *104*, 8–27. https://doi.org/10.1016/j.biopha.2018.05.009.
(2) Conrad, M. D.; Rosenthal, P. J. Antimalarial Drug Resistance in Africa: The Calm before the Storm? *Lancet Infect. Dis.* **2019**, *19* (10), e338–e351. https://doi.org/10.1016/S1473-3099(19)30261-0.
(3) Aguiar, A. C. C.; Panciera, M.; Simão dos Santos, E. F.; Singh, M. K.; Garcia, M. L.; de Souza, G. E.; Nakabashi, M.; Costa, J. L.; Garcia, C. R. S.; Oliva, G.; Correia, C. R. D.; Guido, R. V. C. Discovery of Marinoquinolines as Potent and Fast-Acting Plasmodium Falciparum Inhibitors with in Vivo Activity. *J. Med. Chem.* **2018**, *61* (13), 5547–5568. https://doi.org/10.1021/acs.jmedchem.8b00143.