Design of a combinatorial synthetic route for Tafenoquine derivatives in the search for new chemical hits to prevent relapse of Plasmodium vivax Malaria

Summary: Plasmodium vivax is the most widespread human malaria, there were an estimated 219 million cases and 435,000 related deaths in 2017. This Plasmodium parasite can lie dormant in the liver (in a form known as hypnozoite) from where it periodically reactivates to cause relapses of malaria. Hence, a single P. vivax infection can give rise to multiple episodes of the disease. Tafenoquine is a single-dose 8-aminoquinoline that has recently been registered and approved by the FDA (2018) for the radical cure of P. vivax. This is the first new treatment in six decades for this mosquito-borne disease that can cause acute relapses weeks or months after an insect bite. However, the active principle ingredient (API) of a drug consists in a molecule selected from a large combinatorial library defined by the Markush structure described as a claim in the patent of the drug. By this project, it is expected to demonstrate there is part in this chemical space protected that has not been explored which can hide more active molecules. Therefore, a combinatorial synthetic route is needed to synthesize a rational selection of this library of 8-aminoquinoline derivatives to further test their activity and contrast it with the Tafenoquine in the search for new leads.

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