Design, synthesis and biological study of a universal fluorescent probe for chalcone pharmacology

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Résumé

Chalcones have a plethora of biological activities, but their valorisation as drugs is hampered by their largely unknown mechanisms of action. We have stepwise designed and synthesized a unique benzochalcone fluorescent probe (HAB) endowed with high cell and tissue permeability, optimal photophysics and high quantum yield, as well as sufficiently minimal in structure to allow the pharmacological profiling of representative bioactive chalcones. HAB was validated in microscopic imaging and flow cytometry assays in live murine macrophages and *L. amazonensis* promastigotes. This pharmacological evaluation was based on a differential read-out formed by the association of HAB and competing antileishmanial chalcones, and led to the categorization of a panel of chemically diverse compounds regarding qualitative SARs and target organelles (acidocalcisomes, lysosomes and mitochondria). HAB probe was successfully imaged in live zebrafish (*Danio rerio*) larvae where it proved to be cell- and compartment-specific by targeting the neutrophil granules. However, the probe was not displaced by pharmacologically-relevant competing chalcones in this biological model. In addition to yielding novel paradigms in chalcone structure-fluorescence relationships and live-cell and live-animal chalcone imaging, our study shows that HAB-based fluorescent probes hold promise for the biological and pharmacological study of organelles, cells as well as organisms of biomedical relevance.

Mots-Clés: chalcone, fluorescent probe, Leishmania, zebrafish, imaging

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