Antileishmanial activity of anthranoïds from Psorospermum genus (Hypericaceae) used in traditional medicine and their structural analogues

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Résumé

An ethnopharmacological study allowed the selection of three *Psorospermum* species for the strong antileishmanial activity of their bark extracts. Then phytochemical studies led to the isolation and characterization of several anthranoid compounds active on amastigotes of visceral forms of *Leishmania* (*L. donovani, L. infantum*). Deacetylvismione H exhibited the strongest antileishmanial activity (IC50=0.031 μM against *L. donovani* axenic amastigotes, Selectivity Index=112). The activity seemed to be directed by the nature of the anthranoid moiety and the position and the nature of the substitution groups. In order to understand the mechanism of action and improve both the activity and selectivity of the molecules, we synthesized several analogues of natural anthranoid compounds. One new analogue substituted with a prenyl group on a key position has already been synthetized with improved pharmacological profile (IC50=0.010 μM, SI=401). These data demonstrate for the first time the *in vitro* and *in vivo* antileishmanial effect of natural vismiones. SAR study revealed that vismione core substituted with prenyl group on position 3 and free hydroxyl groups on positions 1, 6 and 9 is strongly associated to antileishmanial activity against visceral species. To find out the mechanism of action *in silico* approaches and proteomic studies are under way.

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Mots-Clés: Antileishmanial activity, Psorospermum, anthranoïds, analogues synthesis, structure activity relationship