

BIOACTIVE FLAVONOIDS FROM THE GENUS *PSOROTHAMNUS*

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The plant genus *Psorothamnus* was identified in our laboratory as a rich source of potential new antiparasitic compounds. In previous work, we isolated antileishmanial and antitrypanosomal compounds from *P. polydenius* that displayed selectivity for these organisms¹. Another member of the same genus, *P. arborescens* exhibited significant activity against *Leishmania donovani* axenic amastigotes and *Trypanosoma brucei brucei*. Bioactivity-guided fractionation of the root extract of *P. arborescens* yielded the new isoflavone, 5,7,3',4'-tetrahydroxy-2'-prenylisoflavone (**1a**), the new 2-arylbenzofuran, 2-(2'-hydroxy-4',5'-methylenedioxyphenyl)-6-methoxybenzofuran, together with seven other known compounds, fremontin, glycyrrhisoflavone, calycosin, maackiain, 4-hydroxymaackiain, isoliquiritigenin, and oleanolic acid. In addition, the structure of the isoflavone fremontin had been revised using spectroscopic and chemical methods. The isoflavone **1a** and isoliquiritigenin displayed leishmanicidal activity with IC₅₀ values of 4.6 and 5.3 µg/mL, respectively, against *L. donovani* axenic amastigotes. Calycosin exhibited selective toxicity against *T. b. brucei* (IC₅₀ 3.6 µg/mL) compared to *L. donovani* amastigotes and Vero cells (IC₅₀ 28.5 and 45.1 µg/mL, respectively). These results prompted us to test a small group of structurally-related isoflavones for their antitrypanosomal activities. Genistein and 7,3',4'-trihydroxyisoflavone displayed promising activity (IC₅₀ values 1.1 and 1.9 µg/mL, equivalent to 4.2 and 7.1 µM, respectively) and selectivity (IC₅₀ versus Vero cells: 33 and 135 µM, respectively). This study suggest that the isoflavone skeleton deserves further investigation as a template for novel antileishmanial and trypanocidal compounds

1. Salem, M. M. and Werbovetz, K. A. (2005) *J. Nat. Prod.* 68(1), 108-111.