A251 Structures and biological activities of constituents from *Brosimum acutifolium*

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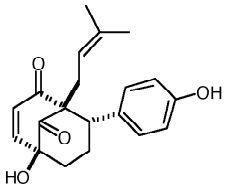
In the course of a screening program to discover new lead compounds from Brazilian Medicinal Plants, we investigated the constituents of bark of *Brosimum acutifolium* (Moraceae), popular name "Murure". This plant has been used in folk medicine in the Amazonian region as an anti-inflammatory and anti-rheumatic agent. The methanol extract of *B. acutifolium* was partitioned between ethyl acetate and water. The ethyl acetate extract was subjected to column chromatography and further purified by HPLC. Seventeen new flavonoids and one new lignan were isolated with known fifteen compounds. The structures of these compounds were elucidated by spectroscopic methods. One of the new flavonoids has a unique rearranged carbon skeleton (**1**) and two of them have novel structures consisting of catechin and phenylpropanoid moieties (**2**, **3**). Some of those flavonoids showed inhibitory effects against protein kinase A or C.



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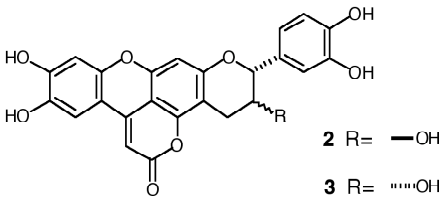

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A252 O-Galloyl flavonoids from *Geranium pyrenaicum* and their *in vitro* antileishmanial activity

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In Turkish folk-medicine, the aerial parts of some species, known as "Turnagagasi", form the basis of a number of herbal preparations (1). Among these traditionally used Geranium species is *G. pyrenaicum* Burm. fil. (Geraniaceae). No phytochemical study on this species has so far been reported. Fractionation of the ethyl acetate soluble portion of the aerial parts of *G. pyrenaicum* by a combination of chromatography on Sephadex LH-20 using water-methanol gradients and preparative TLC separations afforded a series of flavonoids including six known flavonol glycosides [kaempferol 3-O-β-glucopyranoside (**1**), quercetin 3-O-β-glucopyranoside (**2**), quercetin 3-O-β-galactopyranoside (**3**), kaempferol 3-O-(2"-O-galloyl)-β-glucopyranoside (**4**), quercetin 3-O-(2"-O-galloyl)-β-glucopyranoside (**5**), quercetin 3-O-(2",3"-di-O-galloyl)-β-glucopyranoside (**6**)] and the new natural flavonol derivative, kaempferol-3-O-(2",3"-di-O-galloyl)-βglucopyranoside (**7**). Noteworthy is that compound **6** represents a rarely found metabolite, its occurrence being hitherto confined to *Euphorbia maculata* (2). The structures of these compounds were established from spectroscopic studies.

As part of our ongoing research directed toward the isolation and identification of antileishmanial products, the isolates **1-7** were evaluated for their *in vitro* leishmanicidal activities against extracellular promastigotes of *Leishmania major*, *L. donovani* and *L. amazonensis*, and against their intracellular amastigote forms residing within RAW 264.7 cells. With IC_{50} values ranging from 3.3 - 31.5 nM, all compounds showed fairly high antileishmanial activity against the amastigotes, when compared with the IC_{50} value 10.6 nM of the reference drug Pentostam®. In contrast, none of these compounds showed selective cytotoxicity against promastigotes and the mammalian host cell.

References: 1. Baytop, T. (1984) Therapy with Medicinal Plants in Turkey (Past and Present), Istanbul University Publication No 3255, Istanbul. **2.** Amakura, Y. et al. (1997) Can. J. Chem. 75: 727.